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BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 18 1950

FREEZING AND DESICCATION OF MOUSE TUMOURS*

BY

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[WITH SPECIAL PLATE]

Gye and his colleagues (Gye, 1949; Gye, Begg, Mann, and Craigie, 1949; Mann, 1949b, 1949c; Mann and Dunn, 1949) published a series of experiments on the propagation of mouse tumours, first by frozen and then by frozen and desiccated tumour tissues. As the result of these experiments they arrived at the following conclusions: (*a*) that freezing alone is sufficient to kill tumour cells, and more effective still is freezing followed by drying; and (*b*) that the newly induced tumours must have been initiated by a virus, since frozen and frozen-and-dried tumour material is able to induce tumours on inoculation.

In view of the interesting experimental evidence and the far-reaching conclusions based on it, experiments were undertaken (*a*) to repeat the observations described by Gye *et al.* with their own and other tumours, and (*b*) to test their claim to have obtained evidence of a cancer virus.

The technique followed throughout the experiments was, in essence, that described by the above authors. The pump employed was the "Speedivac" Model 2 two-stage rotary vacuum pump, which gives a vacuum of 0.00001 mm. Hg and has a displacement of 48 litres a minute (W. Edwards & Co., Ltd.). No estimate of the weight of the dried material was made by Gye *et al.* so far as can be judged from their publications. They report no attempts to dry their material to a constant weight, and we know of none. Gye (1948–9, page 13) states that Craigie's apparatus "dries a gramme of finely divided tumour tissue in less than an hour," and that "the tissues have been dried to dust." In another experiment Gye (1948–9, page 14) refers to "fine dry scales of tissue" after drying for 130 minutes. As these were the only criteria of dryness described by him we accepted and adopted them. In most of the present experiments 5.3% glucose solution was used as a diluent fluid in quantities either equal to, or up to three times, the weight of the tumour material, usually 1 g. The drying-time varied according to the amount of tissue and diluent in the container. The desiccation process was usually carried on for 3½ hours. The dried material was reconstituted in 5.3% glucose solution or in 1 in 500 neutral solution of cysteine or in a fluid composed of equal quantities of 5.3% glucose solution and cysteine solution, all added in amounts from three to five times the original volume of the tumour-cell suspension. The resulting suspension was injected into the mice by various routes in quantities varying from 0.1 to 0.5 ml.

It was found that there was no difficulty in repeating the results of Gye *et al.*, both those of freezing and those of freeze-drying the various sarcoma tissues employed in the present experiments.

1. Experiments with Mouse Sarcomata

The results are set out in Table I. The failure to obtain tumours in the first two experiments with the 37S tumour may have been due partly to faulty technique or to the condition of the tumour tissue, while the negative result with the Crocker sarcoma may have been due to a temporary breakdown in the supply of solid CO_2, when the temperature in the insulated box rose to $-12°$ C. The negative results with these two tumours will be referred to in the section on histology.

2. Experiments with Mouse Breast Carcinomata

Employing the same technique we found that the breast carcinomata do not stand up to the conditions of the experiment in the same way as do the sarcomata. The results both of freezing and of freezing followed by desiccation of mouse mammary carcinomata are presented in Table II.

It will be seen that while the results with the carcinomata are not as good as those with the sarcomata, they suffice to confirm the observations of Mann (1949b) and Mann and Dunn (1949). Altogether seven experiments were carried out—three with spontaneous C3H breast carcinomata and four with transplantable C3H breast carcinomata. While it must be admitted that the number of experiments is too small from which to draw any final conclusion about a possible difference between transplantable and spontaneous

*Preliminary demonstration given at the Second Informal Conference of the Northern Cancer Research Workers on Normal and Abnormal Cell Growth held at Leeds on September 24–25, 1949, and communicated to: (1) the Pathological Society of Great Britain and Ireland in London, January 7, 1950; (2) the Joint Meeting of the Netherlands Pathological Society and the Pathological Society of Great Britain and Ireland held in Leyden, April 14, 1950; (3) the Conference on the Freezing and Drying of Animal Cells at the National Institute of Medical Research, London, June 28, 1950; and (4) the 5th International Cancer Congress, Paris, July 16, 1950.

TABLE I.—*Freezing, and Freezing Followed by Desiccation, of Different Sarcomata*

Strain	Tumour	Diluent	Time Frozen	Desiccation Time	Method of Inoculation	Mice		No. of Tumours	Time of Appearance	Time of Observation	Histology	Remarks
						Sex	No.					
(C57 x A) F_1	37 sarcoma	None	30 days	Not done	Subcutaneous	M, F	10	0	—	11 weeks	Not done	—
,,	,,	,,	30 ,,	,,	Intrapleural	M, F	4	0	—	7 ,,	,,	—
,,	,,	,,	30 ,,	,,	Intraperitoneal	M, F	5	5	1–3 weeks	7 ,,	,,	—
,,	,,	,,	74 ,,	3½ hours	Subcutaneous	M	10	5	2–3 ,,	5 ,,	,,	5·3% glucose added before desiccation
C57 ..	C48 sarcoma	5·3% glucose	51 ,,	Not done	,,	M	3	3	5–8 days	3 ,,	Done	—
,,	,,	,,	51 ,,	,,	Intraperitoneal	M	3	3	5–8 ,,	3 ,,	,,	—
,,	,,	,,	51 ,,	3½ hours	Subcutaneous	M	3	2	2–5 weeks	7 ,,	,,	Desiccated tissue reconstituted in cysteine
,,	,,	,,	51 ,,	3½ ,,	Intraperitoneal	M	2	2	3 ,,	7 ,,	,,	,, ,,
,,	,,	,,	27 ,,	3½ ,,	Subcutaneous	M	18	18	1–2 ,,	3 ,,	,,	Desiccated tissue reconstituted in 5·3% glucose
C3H ..	C3H sarcoma	,,	7 ,,	3½ ,,	,,	M	7	4	2–3 ,,	4 ,,	,,	,, ,,
,,	,,	,,	10 ,,	2 ,,	,,	M	12	11	1 week	2 ,,	,,	Desiccated tissue reconstituted in equal volumes of 5·3% glucose and cysteine
,,	,,	,,	12 hours	1 hour	,,	M	6	6	4–5 days	2 ,,	,,	Desiccated tissue reconstituted in 5·3% glucose
RIII ..	RIII (No. 4) sarcoma	,,	87 days	3½ hours	,,	M, F	12	12	2 weeks	4 ,,	,,	,, ,,
(C57 x A) F_1	Crocker sarcoma	,,	107 ,,	Not done	,,	M, F	12	0	—	5 ,,	,,	—

TABLE II.—*Freezing, and Freezing Followed by Desiccation, of Mammary Carcinomata.*

Strain	Tumour	Diluent	Time Frozen	Desiccation Time	Method of Inoculation	Mice		No. of Tumours	Time of Appearance	Time of Observation	Histology	Remarks
						Sex	No.					
C3H ..	C3H spontaneous breast carcinoma	None	13 days	Not done	Subcutaneous	M	12	2	2–3 weeks	12 weeks	Not done	—
,, ..	,,	Physiological saline	13 ,,	,,	,,	M	6	4	4–8 ,,	14 ,,	,,	—
..	C3H transplantable breast carcinoma	None	30 ,,	,,	,,	M	12	0	—	12 ,,	,,	—
,, ..	,,	,,	30 ,,	,,	Intrapleural or intraperitoneal	M	6	0	—	12 ,,	,,	—
,, ..	,,	5·3% glucose	19 ,,	,,	Intraperitoneal	M	11	0	—	17 ,,	Done	—
,, ..	,,	None	74 ,,	3½ hours	Subcutaneous	M	12	0	—	12 ,,	Not done	Desiccated tissue reconstituted in 5·3% glucose
,, ..	C3H spontaneous breast carcinoma	5·3% glucose	11 ,,	3½ ,,	,,	M	3	1	8 weeks	12 ,,	Done	,, ,,

carcinomata in the resistance to freezing and drying, attention might be drawn to the results of Klinke (1940) and Cramer (1930), who similarly observed that spontaneous mammary carcinomata showed a greater resistance to cold (−196° C.) than transplantable breast carcinomata.

It is not altogether surprising that the sarcomata should withstand the treatments of freezing and of freeze-drying better than the carcinomata. The carcinomata as a whole are derived from more highly differentiated tissues than the sarcomata, and it would not be unreasonable to expect them to be more susceptible to adverse conditions. Certainly in our experiments there were more visible changes, suggesting cell damage, to be found microscopically in the case of the carcinomata than in the sarcomata; it may not be unreasonable to associate this fact with the experimental results.

Centrifugation of Frozen and Frozen-desiccated Material

Having satisfied ourselves that the results described by Gye *et al.* can be repeated at will, not only with the same but also with different tumours, we undertook an experiment to test whether an active agent or virus could be separated from the tumour cells or whether the tumour-inducing activity is associated with the tumour cells themselves.

Suspensions of minced tumour tissues which had been previously frozen, or frozen and dried, and then reconstituted were centrifuged at 3,000 to 7,000 times gravity for periods of time varying from two to five minutes. Such centrifugation is insufficient to remove viruses from fluid suspensions, and it is reasonable to expect that any virus present would remain in the supernatant fluid. Our aim was to obtain at least a partial separation of virus from the tumour cells, and to test the two resulting fractions for activity by inoculation. The results of inoculation of the sediment and of the supernatant fluids are shown in Tables III and IV.

As can be seen from these tables, tumours were induced in each case with the sediment obtained after centrifugation of the various tumour suspensions, and in no case were tumours observed following inoculation of the water-clear supernatant.

Table IV demonstrates the greater susceptibility to the combined treatment of cold and drying that was noticed in the mammary carcinomata as compared with the sarcomata. Only one tumour was induced by the carcinomata, and in this case by the sediment.

Thus from these centrifugation experiments it is quite clear that the power of tumour suspensions, whether frozen or frozen and then dried, to induce tumours remains with

TABLE III.—*Centrifugation of Frozen and Frozen-desiccated Sarcomata.*

Strain	Tumour	Diluent	Time Frozen	Desiccation Time	Centrifugation	Method of Inoculation	Mice		No. of Tumours	Time of Appearance	Time of Observation	Histology	Remarks
							Sex	No.					
(C57 x A) F_1	37 sarcoma	None	30 days	Not done	3,000 × g. 5 minutes	Subcutaneous supernatant	M, F	11	0	—	11 weeks	Not done	Centrifuged in 5·3% glucose
,,	,,	,,	30 ,,	,,	,,	Subcutaneous sediment	M, F	10	4	3–4 weeks	11 ,,	,,	,,
,,	,,	5·3% glucose	18 ,,	3½ hours	7,000 × g. 3 minutes	Intraperitoneal supernatant	M	7	0	—	9 ,,	Done	Desiccated tissue resuspended in cysteine
,,	,,	,,	18 ,,	3½ ,,	,,	Intraperitoneal sediment	M	9	3	5–13 days	9 ,,	,,	,,
C57 ,,	C48 sarcoma	,,	51 ,,	Not done	3,500 × g. 5 minutes	Subcutaneous supernatant	M	2	0	—	12 ,,	,,	—
,,	,,	,,	51 ,,	,,	,,	Intraperitoneal supernatant	M	4	0	—	12 ,,	,,	—
,,	,,	,,	51 ,,	,,	,,	Subcutaneous sediment	M	2	2	5–9 days	3 ,,	,,	—
,,	,,	,,	51 ,,	,,	,,	Intraperitoneal sediment	M	4	4	9–13 ,,	3 ,,	,,	—
,,	,,	,,	51 ,,	3½ hours	7,000 × g. 5 minutes	Subcutaneous supernatant	M	6	0	—	12 ,,	,,	Desiccated tissue reconstituted in cysteine
,,	,,	,,	51 ,,	3½ ,,	,,	Subcutaneous sediment	M	9	6	4–5 weeks	12 ,,	,,	,,
C3H ,,	C3H sarcoma	,,	30 ,,	3½ ,,	7,000 × g. 2 minutes	Subcutaneous supernatant	M	6	0	—	12 ,,	,,	Desiccated tissue reconstituted in 5·3% glucose
,,	,,	,,	30 ,,	3½ ,,	,,	Subcutaneous sediment	M	12	10	2 weeks	4 ,,	,,	,,
(C57 x A) F_1	Crocker sarcoma	,,	22 ,,	3½ ,,	7,000 × g. 3 minutes	Subcutaneous supernatant	M, F	16	0	—	16 ,,	,,	Desiccated tissue reconstituted in equal quantities of glucose and cysteine
,,	,,	,,	22 ,,	3½ ,,	,,	Subcutaneous sediment	M, F	22	16	1–3 weeks	9 ,,	,,	,,

TABLE IV.—*Centrifugation of Frozen and Frozen-desiccated Breast Carcinomata.*

Strain	Tumour	Diluent	Time Frozen	Desiccation Time	Centrifugation	Method of Inoculation	Mice		No. of Tumours	Time of Appearance	Time of Observation	Histology	Remarks
							Sex	No.					
C3H ,,	C3H transplantable breast carcinoma	None	30 days	Not done	7,000 × g. 5 minutes	Subcutaneous supernatant	M	12	0	—	11 weeks	Not done	Centrifuged in 5·3% glucose
,,	,,	,,	30 ,,	,,	,,	Subcutaneous sediment	M	12	0	—	11 ,,	,,	,,
,,	,,	5·3% glucose	38 ,,	3½ hours	7,000 × g. 3 minutes	Subcutaneous supernatant	M	9	0	—	18 ,,	Done	Desiccated tissue resuspended in equal volumes of glucose and cysteine
,,	,,	,,	38 ,,	3½ ,,	,,	Subcutaneous sediment	M	9	0	—	18 ,,	,,	,,
,,	,,	,,	25 ,,	3½ ,,	7,000 × g. 2 minutes	Subcutaneous supernatant	M	7	0	—	21 ,,	Not done	,,
,,	,,	,,	25 ,,	3½ ,,	,,	Subcutaneous sediment	M	10	1	14 weeks	21 ,,	,,	,,

the tumour cells. Everything points to the activity being associated with the cellular material, alive or dead, as it is never found in the clear cell-free supernatant, as might reasonably be expected if the action were the results of a virus. A reasonable deduction from this observation is that some tumour cells may survive the treatment and thus be responsible for the transmission of tumours. Histological study greatly strengthens this deduction.

Histological Investigations

Gye *et al.* (1949) stated that the results of their histological examinations of random samples of cell suspensions had failed to support the idea of cell survival. Dried tissues examined by them "showed only a mass of debris and shrunken nuclei." In their papers there is little information about histological appearance, and in none of them do they present any illustration, nor is there any description, of the appearances of frozen and dried tumour material fixed *after* reconstitution. Mann and Dunn (1949) reproduce a photograph of a mammary carcinoma fixed immediately after freezing followed by desiccation but *before* reconstitution, although there is no figure to illustrate the same tissue fixed *after* reconstitution.

In each of the present experiments the minced tumour tissues were fixed in Bouin's fluid, stained with haematoxylin and eosin, and examined microscopically: (1) before freezing, (2) after freezing in 5.3% glucose, (3) after freezing followed by drying *before* reconstitution, and (4) after combined freezing and drying *after* reconstitution in glucose or cysteine.

The results are shown in Figs. 1–20 (see Plate). It is difficult to detect any differences in the appearance of many of the sarcoma cells before and after freezing (see Figs. 4 and 5). Similarly, after freezing and desiccation followed by reconstitution, the suspensions of sarcoma cells had an appearance similar to that of the same suspensions before freezing and drying (see Figs. 1 and 2, 4 and 7, 9 and 10, 11 and 13, and 14, 18, and 20).

However, in no case could intact cells be found after freezing and drying but *before* reconstitution: this observation agrees entirely with that described by Gye *et al.* (1949) (see Figs. 6, 12, and 19) in revealing "only a

mass of debris and shrunken nuclei." The addition of any of the mentioned diluents to the frozen and desiccated material *before* fixation in Bouin's fluid creates an amazing and dramatic effect on the fixed tissues (see Figs. 6 and 7, 12 and 13, and 19 and 20). Many of the tumour cells are, to all appearances, intact, resembling in their entirety the tumour cells before the treatment.

How it can have come about that Gye *et al.* (1949) and Mann and Dunn (1949) omitted this step is not clear; but it is a matter for conjecture whether the failure to observe the appearances of frozen and dried tissue *after* reconstitution might not have been one of the reasons for their interpretation of the results.

While the microscope cannot with certainty reveal if tumour cells are alive or dead, the appearance of tumour-cell suspensions obtained before and after freezing, or freezing followed by drying, strongly suggests that some of the tumour cells might have been alive and have been responsible for the induction of tumours either with frozen or with frozen-and-dried material. From the appearance of the tumour cells there is no evidence that they are dead. The biological results in every case support the inferences which might reasonably be drawn from the microscopical appearances. Thus in every case in which the tumours were obtained by inoculation with the treated material the microscope suggested that at least many cells might be alive: certainly they seemed very little altered when compared with the fresh tumour-cell suspension; while, in those cases in which the biological tests were negative, histological examination showed considerable cell injury or even loss of cell structure. This was particularly well shown in the experiments with the Crocker sarcoma (Fig. 3) and with 37S (Fig. 8). In the Crocker suspension, frozen for 107 days, no intact cells were seen and no tumours were induced, while the 37S tumour suspension, which presented profound cellular changes, gave fewer tumours than suspensions of other tumours treated in a similar manner. Again, in the case of C3H mammary carcinomata similar changes, indicative of cell injury, could be seen both in the frozen and in the frozen-desiccated material, which goes hand in hand with the erratic results obtained with the C3H mammary carcinomata, especially the transplantable one (see Figs. 15, 16, and 17).

To sum up, it might in general be said that, viewing the results of the microscopical studies as a whole, the material which presents little histological evidence of cell damage can be relied upon to induce tumours more readily than that which has a damaged appearance.

Discussion

(a) Freezing and Drying

If there has been no difficulty in repeating the experiments of Gye *et al.* (Table V), the same cannot be said of accepting their interpretation—namely, that these experiments indicate a virus to be the cause of the successful transmission of tumours by frozen-and-dried material. Before discussing the reasons for the inability to agree with Gye's conclusions, experiments in this field by previous workers will be described and discussed. It is felt that a careful perusal of some of the available experiences of previous workers should in itself command the greatest caution in accepting the conclusions reached by Gye *et al.*, because in the literature there is ample evidence that extremes of cold, far beyond anything employed by Gye, can be successfully resisted by some organisms without jeopardizing life.

Gye *et al.* were obviously very much impressed with the inferences which they had drawn from experiments

TABLE V.—*Summary of Results*

Tumour	Freezing Alone	Freezing and Desiccation	Centrifugation	No. of Mice	No. of Tumours
37 sarcoma ..	+	−	−	19	5
,, ..	−	+	−	10	5
,, ..	+	−	Supernatant	11	0
			sediment	10	4
,, ..	−	+	,,	7	0
				9	3
C48 sarcoma ..	+	−	−	6	6
,, ..	−	+	−	23	22
,, ..	+	−	Supernatant	6	0
			sediment	6	6
,, ..	−	+	,,	6	0
				9	6
Crocker sarcoma	+	−	−	12	0
,, ..	−	+	Supernatant	16	0
			sediment	22	16
C3H sarcoma..	+	−	−	25	21
,, ..	−	+	Supernatant	6	0
			sediment	12	10
RJII (No. 4) sarcoma ..	+	−	−	12	12
C3H spontaneous breast carcinoma ..	+	−	−	18	6
,, ..	−	+	−	3	1
C3H transplantable breast carcinoma ..	+	−	−	29	0
,, ..	−	+	−	12	0
,, ..	+	−	Supernatant	12	0
			sediment	12	0
,, ..	−	+	,,	16	0
				19	1

+ Denotes procedure carried out. − Denotes procedure not carried out.

of Ida Mann (1949a), in which she found that embryonic tissues of mice do not survive exposure to freezing at −79° C. for one hour. But surely there was nothing new in this, as many previous observers had already published work of a similar nature. Thus Gaylord (1908) was not able to obtain subcutaneous transplantation of mouse embryo epithelium after exposure to −180° C. Lambert (1912) observed that chick embryos developed after exposure to −5° C. for 10 days, and that chick embryo heart was killed after one minute at −74° C., but survived at −20° C. for five minutes. Simonin (1931) found that fragments of mouse and rat embryo survived for five days at −5° C., but were killed at −15° C.

There are numerous publications on the storage of tumour tissues at low temperatures for periods varying up to two years, and a successful transplantation of such tissues into animals. The methods employed by different authors were extremely variable: long exposure to only a few degrees of cold, short exposure to very low temperatures, and single or repeated exposures to various temperatures have all been described for various types of tumours, usually with a great measure of success.

Michaelis (1905) was the first to observe the survival of Jensen rat sarcoma after exposure to liquid air for 30 minutes. Ehrlich (1907) reported survival of carcinoma cells after storage at −8° C. for two years and after 48 hours at 38° C. Salvin-Moore and Walker (1908) exposed a transplantable mouse mammary carcinoma to liquid air for 30 minutes, and succeeded in transplanting it. Salvin-Moore and Barret (1908) observed similar results after exposure of mouse sarcoma and carcinoma to liquid air for 20 minutes. Gaylord (1908) confirmed these findings. Cramer (1930) froze finely minced tissues of seven different mammalian tumours in CO_2 and found that sarcomata grew and carcinomata failed to grow on transplantation following this treatment. Some of the tumours (37S) induced tumours after freezing and thawing repeated eight times. Auler (1932) found that Ehrlich mouse carcinoma grew on transplantation after an exposure to −73° C. for 25 minutes, and Jensen rat sarcoma after five minutes at −73° C., and that Flexner–Jobling carcinoma failed to grow.

Barnes and Furth (1937) and Breedis, Barnes, and Furth (1937) successfully transplanted leukaemia of mice after exposure to −70° C. for 56 days and also a similarly treated sarcoma induced by benzpyrene. Breedis and Furth (1938) reported the survival of various tumours (sarcomata and carcinomata) after storage at −79° C. for 400 days. Klinke (1937) demonstrated successful transplantation of many mice and rat tumours after direct exposure to −196° C. for periods up to 47 hours. The only observed difference between tumours treated in this way and the controls was the delay in tumour appearance after freezing. Mider and Morton (1939) reported that Walker rat carcinoma and 37S and 180 mouse sarcomata grew on subcutaneous transplantation after exposure to −79° C.

Klinke (1940) succeeded in demonstrating growth in tissue culture of Ehrlich mouse sarcoma after exposure to −253° C. lasting 10 minutes, and of Jensen rat sarcoma after two days at −196° C. Although intact cells could be seen in tissue culture of a transplantable breast carcinoma after exposure to these temperatures, growth was not obtainable. Klinke concluded that exposure to low temperatures gives no basis for the existence of a virus in mammalian tumours because of the results of vital staining and growth in tissue cultures. Subsequent to Gye's papers, Craigie (1949a, 1949b, 1949c) with proper caution suggested that there may be some cell survival following freezing of tumour cells in a mixture of dextrose and 40% glycerol. Of all these results, Klinke's (1940) obtained after exposure of tumour cells to low temperature are perhaps the most pertinent, as he clearly demonstrated the survival and growth *in vitro* of tumour cells which had been so exposed. This property of survival following exposure to cold is not limited to tumour cells, as can be seen from the quoted literature.

Not only does the literature abound in examples of the survival of tumour cells after extremes of freezing, but there are many references to the ability of normal cells, tissues, and organisms to survive such treatment. Luyet and Gehenio (1938a) reviewed the experiments on survival of unicellular and other primitive organisms after freezing. Heilbrunn (1943) also reviewed experiments on the resistance of single-celled and multicellular animals and plants to very low temperatures. It is now known that some organisms can withstand temperatures close to the absolute zero, while others are killed at temperatures above the freezing-point of water, but the rate at which an organism is cooled and the rate at which it is brought back to higher temperatures is known to affect the ability of the organism to withstand the cold to which it is subjected.

De Jong (quoted by Heilbrunn) observed that trypanosomes are able to resist exposure to −190° C. Rahm (1922) demonstrated that nematodes, rotifers, and tardigrades placed in water cooled gradually could be brought to the temperature of liquid hydrogen (−253° C.) without death, but that they died when brought to that temperature suddenly. Luyet and Gehenio (1938b) reported survival of plant cells after exposure to liquid air, and Luyet and Hartung (1941) demonstrated survival of common vinegar eels (*Anguilla aceti*) after immersion in liquid air (−190° C.), preceded by immersion in 30% ethylene glycol solution, and rapid rewarming in water at 30° C. They reported that in one experiment they had observed a vinegar eel after freezing in liquid air give birth to a live offspring, which survived two weeks. Breedis and Furth (1938) reported survival of chicken epithelium after exposure at −79° C., Mider and Morton (1939) the survival of squamous epithelial cells of homologous skin grafts in the rat, and Briggs and Jund (1944) survival of normal mouse skin after exposure to −79° C. for one hour. Webster (1944) described survival of human skin on grafting after exposure to −72° C. for periods up to 17 days, and, what is even more interesting, after drying in the frozen state. Blumenthal and Walsh (1950) have recently demonstrated the survival of guinea-pig thyroid and parathyroid in auto-transplants exposed to −190° C.

There is besides a large body of work on the survival of spermatozoa following extremes of low temperatures, and even after freezing and drying. Davenport (1897) possibly was the first to show the resistance of human spermatozoa to low temperatures. Jahnel (1938) demonstrated the resistance of human spermatozoa to −196° C. and even to −269.5° C. The spermatozoa showed motility after 52 hours at −196° C., also after exposure to −79° C. for 40 days or to −269.5° C. for three hours. Weber (1938) observed motility of bull spermatozoa after 96 hours at 0° C. Luyet and Hodapp (1938) found that frog spermatozoa, and Shaffner, Henderson, and Card (1941) that fowl spermatozoa, are resistant to exposure to liquid air. Shettles (1940) observed that human spermatozoa show motility after exposure to −79° C. for up to two months, and to −196° C. (liquid nitrogen) or −269° C. (liquid helium) for five minutes. He also noted individual variation in the sensitivity of various samples of human spermatozoa to these three temperatures. Morphologically they appeared to be in good condition, and continued their motility for several hours; after freezing and drying the morphology of spermatozoa was preserved in his hands, but there was no motility. Hoagland and Pincus (1942) confirmed this observation and reported survival of 67% human spermatozoa after exposure to −195° C. Polge, Smith, and Parkes (1949) observed survival of fowl spermatozoa diluted in equal parts of Ringer's solution containing 40% glycerol at −79° C. for 20 minutes, and after freeze-drying for three hours at −25° C. in 20% glycerol in Ringer's solution.

Altogether from previous work it is crystal clear, therefore, that normal and tumour tissues can withstand freezing, even if embryo tissues cannot: yet in the face of the published evidence Gye (1949) definitely states: "The final conclusion we have reached from these studies is that malignant cells, like embryonic cells, are readily killed by extreme cold. . . ."

(b) Virus Claim

Gye (1949), Gye *et al.* (1949), Mann (1949b, 1949c), and Mann and Dunn (1949) claimed that their successful induction of tumours, after preliminary freezing or freeze-drying of tumour-cell suspension, was due to a tumour-inducing virus. Having decided that freezing and freeze-drying killed the cancer cell, they deduced that the ability of the frozen tumours to induce fresh tumours must have been due to a virus, the activity of which had not been destroyed. So far as can be ascertained from their published papers, this was a deduction from a limited observation. For Gye *et al.* carried out no experiments to separate the supposed virus from the cellular material, nor did they test biologically for the presence of life in the tumour cells after freezing or freeze-drying. But it is an established fact that successful implantation of cellular material is a sound test for cell life, and the simplest interpretation of their results is that the material which they were transplanting contained living cells. There was no need to invoke the presence of a virus.

Subsequent to the original papers (Gye, 1949; Gye *et al.*, 1949) Craigie (1949c) differed from the original view about desiccation as expressed therein. He considers the possibility that a few cells (about 1 in 1,000,000) survive desiccation. But it is still not clear, at least to us, that he

considers, as we do, that the surviving cells are responsible for the tumours induced with frozen-dried material.

Apparently Gye *et al.* made no attempt to look for a virus with the electron microscope, which in these days is perhaps the method *par excellence* for the detection of viruses. For what the observation is worth, we have found that such tumours as have been examined in low-cancer strains, whether induced or spontaneous, are free of any virus-like particles under the electron microscope, whereas in high-breast-cancer strains the electron microscope has consistently revealed the presence of particulate matter mainly of some 250 Å (Passey, Dmochowski, Astbury, and Reed, 1947; Passey, Dmochowski, Astbury, Reed, and Johnson, 1948, 1950; Passey, Dmochowski, Reed, and Astbury, 1950), which is always associated with the Bittner agent.

To sum up: first, in none of our centrifuge experiments were tumours induced with clear supernatants free from cells, while with few exceptions the sediments, in which apparently intact cells were always to be found, regularly induced tumours, which is clear evidence that the tumour-inducing activity was always associated with the tumour cell, and was not separable from it; secondly, the microscopical evidence provides further support for the belief that some of the cells had survived, in that, after the various treatments of freezing and freeze-drying, many intact cells were to be found which in appearance were very little different from the untreated minced material. It seems to us, in view of the available evidence, that there is no need to invoke a virus as the active agent.

It must, however, be admitted that a final decision on whether the cells are viable and are responsible for the results can be reached only after an attempt to grow tumour cells *in vitro* after freeze-drying. Experiments along these lines have been carried out in this department in collaboration with Dr. I. Lasnitzki, from the Strangeways Laboratory, Cambridge. The results of these experiments are reported in the paper which immediately follows this communication.

Summary and Conclusions

Minced tumours, both sarcomata and carcinomata, retain their power to induce fresh tumours after freezing and subsequent desiccation under the experimental conditions described by Gye *et al.*

Centrifugation at slow speeds of tumour tissues similarly treated, together with our histological studies, indicates that living cells, and not a virus, are responsible for the results.

We should like to express our thanks and appreciation to Mr. W. Blackledge, in charge of the photography department of Leeds University, for his help and great care in taking photographs of the histological specimens. We also wish to acknowledge the help given by Mr. Kenneth Morton in the preparation and staining of the histological specimens.

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CULTIVATION IN VITRO OF FROZEN AND DESICCATED MOUSE TUMOUR TISSUES*

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[WITH SPECIAL PLATE]

In order to arrive at a final decision on whether the conclusions of the experiments described in the preceding paper (Passey and Dmochowski, 1950), that freezing and dessication do not necessarily kill tumour cells, were sound, it was decided to put the matter to the test of tissue culture. It was, however, fully realized that it is not as delicate a test as the biological one of animal inoculation, as the conditions of growth *in vitro* are, in general, not as good as those *in vivo*.

Method

The tumour used in the present experiments was the C3H sarcoma described in the original experiments by Gye *et al.* (1949). The tumour tissues were minced,

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suspended in various concentrations of glucose (from 5.3% to 40%), frozen to −79° C. in solid CO_2, and stored at this temperature for periods ranging from 12 hours to 25 days. After storage at −79° C. the suspensions of tumour tissues were desiccated for periods varying from 30 minutes to 3½ hours. After desiccation the tumour material was resuspended in glucose of the same concentration as that in which it had been frozen. Part was used for tissue culture, part for histology, and the remainder injected subcutaneously into mice. The cultures were grown by the hanging-drop technique in a medium consisting of equal parts of chick embryo extract and of a mixture of rat and fowl plasma, in the proportion of three parts of rat plasma to two parts of fowl plasma. This medium has, in general, proved very suitable for the cultivation of fresh mammalian tumours.

Results

Thirteen experiments were carried out. The results are shown in the Table, which gives (*a*) the times of freezing and desiccation; (*b*) the amount of tumour material and the concentrations of glucose in which it was frozen, desiccated, and reconstituted; and (*c*) the behaviour of the tissue, both *in vivo* and *in vitro*.

Type of Tumour	Weight of Tissue/Amount of Glucose	Concentration of Glucose	Time of Freezing	Time of Desiccation	Growth *in vitro*	No. of Mice Injected	No. of Tumours	Time of Appearance of Tumours	Time of Observation	Histology after Desiccation and Reconstitution
C3H sarcoma ..	0·4 g./6·0 ml.	5·3%	12 hours	½ hour	—	6	6	4–7 days	7 weeks	Cells undamaged
,, ..	0·4 g./1·0 ml.	,,	12 ,,	1 ,,	—	4	2	14 ,,	9 ,,	Some cells damaged
,, ..	0·3 g./0·5 ml.	,,	12 ,,	1 ,,	+	17	16	5–7 ,,	3 ,,	Cells undamaged
,, ..	1·7 g./3.5 ml.	,,	10 days	2 hours	—	12	10	7 ,,	4 ,,	Some cells damaged
,, ..	0·6 g./1·5 ml.	,,	25 ,,	2 ,,	—	6	1	14 ,,	4 ,,	Many cells damaged
,, ..	0·7 g./1·5 ml.	,,	7 ,,	3½ ,,	—	5	4	2–3 weeks	4 ,,	Some cells damaged
,, ..	0·4 g./1·5 ml.	10%	12 hours	½ hour	—	6	5	7 days	7 ,,	Cells undamaged
,, ..	0·4 g./1·0 ml.	,,	12 ,,	1 ,,	—	6	3	7 ,,	7 ,,	Some cells damaged
,, ..	0·6 g./1·5 ml.	,,	25 days	2 hours	—	6	0	14 ,,	4 ,,	Majority of cells damaged
,, ..	0·4 g./1·0 ml.	20%	12 hours	½ hour	++	6	4	14 ,,	7 ,,	Cells undamaged
,, ..	0·4 g./1·0 ml.	,,	12 ,,	1½ hours	+	6	3	14 ,,	7 ,,	,, ,,
,, ..	0·6 g./1·5 ml.	,,	25 days	2 ,,	—	5	1	14 ,,	3 ,,	Many cells damaged
,, ..	0·6 g./1·5 ml.	30%	25 ,,	2 ,,	—	6	0	—	9 ,,	Majority of cells damaged
,, ..	0·6 g./1·5 ml.	40%	25 ,,	Not done	Not tested	6	1	16 days	7 ,,	Many cells damaged

In cultures of C3H sarcoma, obtained from fresh tumour material, abundant outgrowth consisting of malignant fibroblasts and macrophages could be seen after one day's incubation. As a rule, rapid liquefaction of the plasma clot took place in the actively growing cultures. Fig. 1 (see Plate), which is a phase-contrast photomicrograph of a living control culture, shows malignant fibroblasts in a zone of liquefaction. In Fig. 2 the edge of a control culture stained with haematoxylin can be seen.

Under the phase-contrast microscope, explants from frozen and desiccated tumour material which has failed to grow showed dark shrunken cells without any structure (Fig. 3). Such explants either do not stain at all or stain very lightly with haematoxylin. In stained specimens the nuclei appear completely amorphous and structureless.

In three experiments successful growth *in vitro* was observed in explants obtained from frozen and desiccated suspensions of tumour cells in glucose solutions. In suspensions of tumour cells in 5.3% glucose solution, frozen for 12 hours and desiccated for one hour, growth occurred in three out of 18 cultures. After 24 hours' incubation the edge of the explant appeared transparent under the phase-contrast microscope, and was composed of healthy cells. At this time many cells had wandered out into the medium (Figs. 4 and 5). This outwandering continued during subsequent incubation, and in spite of exposure to light during photography of the living cultures. After 48 hours' incubation the number of cells seen by means of the phase-contrast microscope had increased markedly (Figs. 6, 7, and 8). The outgrowth consisted of cells of the fibroblast type and some macrophages. Among these malignant fibroblasts binucleate cells could be distinguished.

In suspensions of C3H sarcoma cells in 20% glucose solution, frozen for 12 hours and desiccated for one hour and 15 minutes, growth was obtained in 5 out of 28 cultures (Figs. 9 and 10). The same material desiccated for 30 minutes showed growth in 13 out of 24 cultures (Figs. 11 and 12). In the latter cultures the zone of growth was larger and the cells more numerous, as seen under the phase-contrast microscope, than in those of the same tumour desiccated for 75 minutes. In both cases slender elongated cells of the fibroblast type, many of them binucleate and multinucleate, had grown out from the central explant. Filamentous or short rod-like mitochondria could be seen in the living cultures by means of the phase-contrast microscope. Cell division was present in most cultures, both after 30 minutes' and after 75 minutes' desiccation in 20% glucose. From 15 to 25 mitotic figures were counted in the outgrowth of such cultures. All stages of mitosis, some of them abnormal, could be distinguished (Figs. 13 and 14). Breakage and lagging of chromosomes, bridge-formation in anaphase, polyploidy, and spindle disturbances were observed. Some of the abnormalities probably led to the formation of the binucleate and multinucleate cells present among the resting cells. Liquefaction, which in this tumour is always associated with active growth, was seen in most cultures.

Examination of fixed and stained cultures showed that the central explant consisted of areas of both healthy cells and shrunken debris. This suggests that the unit of survival under the experimental conditions used is not a single cell but that groups of cells survive as a whole. The size of the outgrowth was seen to be in direct proportion to the size of the healthy areas in the central explant.

Discussion

Klinke (1940) demonstrated the survival and growth of tumour cells which had been exposed to low temperatures alone. In the present experiments growth in tissue culture consisting of cell migration and division has been obtained after freezing and desiccation for 30, 60, and 75 minutes. One series of cultures of C3H tumour cells failed to grow *in vitro* under the same conditions as those in which another series, obtained from a different transplant of the same tumour but treated in the same manner, showed outgrowth; this might have been due to the greater viability of the latter. In our hands suspensions of tumour cells desiccated for longer periods than 75 minutes failed to

grow in tissue culture, but induced tumours in mice. This is probably due to the more favourable conditions *in vivo*, which offer better chances of recovery for the treated tumour cells than does the environment *in vitro*; it suggests that successful growth in tissue culture depends on the length of time of desiccation. Although the degree of desiccation reached after 75 minutes may be high, it is realized that dehydration is not complete. If the time of desiccation is more prolonged only few, if any, cells can be expected to survive.

It seems that three stages in the behaviour of tumour cells following different lengths of desiccation can be distinguished: (1) positive growth *in vitro* and *in vivo*; (2) growth *in vivo* but not *in vitro*; and (3) no growth *in vivo* or *in vitro*. Possibly these three stages are related to the amount of water remaining in the tumour material. In this connexion it may be mentioned that, according to Polge, Smith, and Parkes (1949), a high proportion of the water, about 90%, can be withdrawn at low temperatures from fowl semen mixed with equal quantities of 30% glycerol in Ringer's solution without killing the semen. Klinke showed by means of vital staining that the number of living cells in frozen tumour material diminished quickly after thawing followed by incubation in tissue culture. His observation suggests that our failure in tissue culture, especially after the more prolonged desiccations, may also have been due partly to the non-survival of tumour cells during incubation which otherwise would have survived under the more favourable conditions *in vivo*.

As can be seen from the table, the microscopical appearance of tumour cells, after freezing and desiccation and subsequent reconstitution in various solutions of glucose, depended probably on the individual resistance of different samples of tumour cells to the treatment, but to a greater extent on the time of desiccation. Even after the same length of desiccation the number of tumour cells which appeared damaged and the number of tumours induced in mice varied with different samples of tumour material. This may have been the result of the tumours having a different optimum time of freezing and desiccation, owing to their different general condition at the time of the experiment.

The present successful attempts show that tumour cells can withstand a high degree of desiccation when frozen and yet remain viable. They confirm the conclusion reached in the first paper—namely, that the induction of tumours in mice with frozen and desiccated suspensions of tumour cells is due to the proliferation of surviving tumour cells.

Summary and Conclusions

Suspensions of sarcoma cells which have been frozen in glucose solutions and desiccated may show active growth *in vitro* after reconstitution in glucose.

This indicates clearly that some tumour cells survive freezing and desiccation, and that the tumours which develop in mice injected with tumour material which has been frozen and desiccated arise from such surviving cells.

These experiments strengthen the conclusion reached in the first paper, that surviving cells and not a virus were responsible for the results obtained by Gye *et al.*

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CELLULAR TRANSMISSION OF MOUSE SARCOMATA WITH FROZEN-DRIED TUMOUR TISSUES

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[WITH SPECIAL PLATE]

Malignant cells of mouse tumours, after having been frozen to −79° C. and desiccated, have been grown in tissue cultures, as described in the preceding paper (Passey, Dmochowski, Lasnitzki, and Millard, 1950). This is unequivocal evidence of the viability of malignant cells after freezing and drying. There is therefore every justification for assuming that when frozen-dried tumour tissue is inoculated into mice the viable tumour cells present proliferate to form a tumour. Since the validity of this conception is crucial, it seemed desirable that the attempt should be made to confirm it experimentally. Our attention was drawn by Ludford to the advantages, for this purpose, of a technique, devised by Des Ligneris (1930), of grafting tumour tissue in plasma and serum which he described as "*in vitro* culture under *in vivo* conditions." Ludford recommended inoculating frozen-dried tumour tissue in clotted plasma, because he had found that it was possible, after inoculating cells embedded in plasma, to excise the clot after a few days and prepare from it histological sections in which the cells of the inoculum were clearly distinguishable from the surrounding tissues of the host. Experiments were therefore undertaken using this technique concurrently with those described by Passey *et al.* (1950).

Methods

The tumours used in the present experiments were the C3H and C48 sarcomata described in the original experiments of Gye *et al.* (1949) and in those of Passey and Dmochowski (1950) and of Passey *et al.* (1950). The tumour cells, in various concentrations of glucose, were submitted to storage at −79° C. and to desiccation for different lengths of time, followed by reconstitution in glucose of the same concentration as that used initially in each experiment. After reconstitution in glucose, the suspensions of tumour cells were centrifuged for three minutes at 7,000 times gravity, care being taken to keep the time of centrifugation as short as possible so as to avoid damage to cells. After discarding the supernatant fluid, equal amounts of a mixture of rat and fowl plasma (in a proportion of three parts of rat plasma and two parts of fowl plasma) and of chick embryo extract were added to the sediment (usually four to five drops of each) and gently shaken to obtain a suspension of cells in the medium. The suspension of tumour cells in the mixture of rat and fowl plasma and chick embryo extract was then put into an incubator at 37° C. for a few minutes to induce clotting. The clot was then cut into small pieces, some of which were taken for microscopical examination, and the rest grafted subcutaneously into mice by means of a trocar.

The medium used in the experiments was thus the same as that described in the tissue-culture experiments of Passey *et al.* (1950). Similarly, most of the suspensions of tumour cells were the same as those used for the tissue-culture work. Mice were sacrificed at various intervals after grafting and the clots excised and fixed in Bouin's fluid. Serial sections were stained with haematoxylin and eosin.

Eleven experiments with C3H sarcoma and one with C48 sarcoma were carried out. The accompanying Table gives the concentrations of glucose in which the tumour material was suspended, the times of freezing and desiccation, and the results of the microscopical examination of the clots excised at various intervals after grafting.

mass of the implant was necrotic and surrounded by the normal subcutaneous tissue of the mouse. By the fourth day much of the implant was absorbed, and on the fifth, sixth, and subsequent days they observed the beginnings of a new sarcoma in the connective tissue surrounding the necrotic mass. They concluded that "the appearances do not suggest survival of any of the implanted tissue, but rather a fresh sarcomatous reaction of the encapsulating subcutaneous tissues of the host."

In the present experiments these clotted suspensions of tumour cells, which on microscopical examination when first prepared showed few, if any, undamaged cells, appeared as necrotic masses in all subsequent preparations

Sarcoma and Concentration of Glucose	No. of Days Frozen	No. of Hours Desiccated	Result of Microscopical Examination of Clots at Various Time Intervals Following Grafting into Mice											No. of Positive Clots/ No. of Clots Injected
			Original Clot	6 Hours	18 Hours	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	
C3H 5·3%	½	½	+	+	+	−	+	+	+					5/6
"	½	1	+•						∓++	+++	+++	++		11/12
"	½	1	−	−		=	−	−	−					0/6
"	25	2	−			−	−	=	−	−				0/6
C3H 10%	½	½	+		+	∓	∓	−						3/6
"	½	1	+			∓	=	+	−					2/6
"	25	2	−			=	−	=	−					0/6
C3H 20%	½	½	+•			∓	∓	+	−					3/6
"	½	1½	+•			∓	∓	−	+					3/6
"	25	2	−			≡	≡	−	−					0/6
C3H 30%	½	2	−			=	=	=						0/6
C48 5·3%	½	1	+						++++	∓++	++++	+++	+++	17/18

+ Positive clot: contains tumour cells looking apparently unharmed. − Negative clot: no tumour cells apparently unharmed. ∓ Indicates one positive and one negative clot. = or ≡ indicates two or three negative clots. ++ or +++ indicates two or three positive clots. • Grown *in vitro* (Passey *et al.*, 1950).

As can be seen from the photomicrographs (Plate, Figs. 1–4), in many of the clots tumour cells apparently unharmed were found. An increasing number of tumour cells, some of them in division, clearly separated from the surrounding tissues of the mice, were seen in the clots taken out at intervals of 18, 24, 48, 72 hours, 4 days, and on the days following. These clots are designated as positive. Clots in which no apparently unharmed cells were found and which were ultimately absorbed are described as negative. It should be stressed that no actively proliferating cells outside the clots were seen in any of the serial sections. There is no doubt, from the appearance of the tumour cells in the first clots removed and the increasing number of cells in those taken out later, that large tumours would have resulted had growth been allowed to proceed uninterrupted. Growth in tissue culture was obtained only with the C3H tumour in 5.3% glucose frozen for 12 hours and desiccated for one hour, and with the same tumour in 20% glucose, frozen for 12 hours and dried for 30 minutes and 75 minutes (Passey *et al.*, 1950). With the grafted clots positive results were obtained with the same and also with other concentrations of glucose (see Table). The greater number of positive results obtained by inoculating the clotted suspensions of frozen and dried tumour cells into mice is not surprising in view of the more favourable conditions for growth in the animal body. According to Des Ligneris (1930) the medium in which the grafted tumour cells are embedded provides both better nourishment for the cells cut off from the normal circulation and better protection. The tumour cells within the clotted plasma induced no inflammatory reaction. Although a great many of them underwent necrosis, as could be seen in clots removed a day or two after grafting, yet a sufficient number survived and grew to form tumours.

Sections of implants of tumour tissues frozen at −79° C. were examined by Gye *et al.* (1949) at intervals of 2, 3, 4, 5, 6, and 7 days. They found, on the second day, that the made after grafting. They were gradually absorbed *in vivo* and usually disappeared on the fifth or sixth day after transplantation, whereas, as can be seen from Figs. 1–4, clots containing cells looking apparently unharmed when grafted into mice show an increasing number of tumour cells, with many of them in division, when examined at successive intervals after transplantation. No cells outside the clots were actively proliferating, as one would expect if a virus were present capable of diffusing out and infecting the surrounding tissue of the host. Thus the experiments demonstrate that the propagation of tumours with frozen-dried tissue is entirely a process of cellular transmission.

Summary

Suspensions of frozen and desiccated sarcoma cells embedded in clots formed by the addition of chick embryo extract to a mixture of rat and fowl plasmas were inoculated subcutaneously into mice. Sections of clots excised at varying intervals after grafting revealed the presence of viable tumour cells, increasing in numbers with the age of the grafts.

We should like to express our thanks to Dr. R. J. Ludford for his valuable suggestions and helpful advice for carrying out these experiments.

Addendum.—During the preparation of the above paper for publication an additional experiment along similar lines with the C3H sarcoma (0.8 g. of tissue in 1.5 ml. of 5.3% glucose), frozen at −79° C. for 95 days and desiccated for 210 minutes, was carried out. In spite of the prolonged desiccation, an increasing number of tumour cells were seen in the clots taken out at various intervals after grafting. This observation strengthens beyond shadow of doubt the conclusion reached above.

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ATELECTASIS AND BRONCHIECTASIS IN PERTUSSIS

BY

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Laennec in 1819 reported that he had found at post-mortem examination bronchiectasis in the left lower lobe of a child aged 3½ months who had died after an attack of whooping-cough, and stated that he considered the latter disease to be the commonest progenitor of bronchiectasis.

Lander and Davidson (1938) showed experimentally that aspiration of viscid material into peripheral parts of the bronchial tree may be followed by atelectasis and a mechanical compensatory dilatation of the bronchi in the collapsed area. Lander (1946) concluded that when bronchiolar occlusion produces atelectasis with associated bronchial dilatation the following events may take place: (1) the collapsed portion of lung may re-expand, with disappearance of the compensatory bronchial dilatation ("reversible bronchiectasis"); (2) the collapse and consequently the associated bronchial dilatation may be permanent; and (3) the collapsed portion of lung may re-expand, but the bronchi remain dilated because of damage to their walls by infective processes.

Present Investigation

This work affords a ready explanation for the association noted by Laennec between bronchiectasis and pertussis, because in the latter disease, as Erwin (1939) observed, "the tenacious nature of the sputum bespeaks collapse." It was with this in mind that the present investigation was undertaken, though it was not forgotten that Tannenberg and Pinner (1942) and others had shown that bronchiectasis may also be produced by the damming up of secretions distal to obstruction of a main bronchus from intrinsic or extrinsic causes.

With a view to determining the incidence of atelectasis and bronchiectasis in whooping-cough, 150 consecutive cases of this disease admitted to Ruchill Hospital during 1946–7 were examined clinically and radiologically. Cases which arrived gravely ill and died without having full investigation were excluded from the series. The cases were *x*-rayed at weekly intervals, and, when atelectasis was detected or suspected clinically or radiologically, lateral films were taken to verify the diagnosis and define the location. Lordotic as well as lateral views were used when right middle-lobe or lingular collapse was suspected.

In cases showing collapse of marked or moderate extent, and in cases with slight persistent collapse, bronchography was carried out except in children under 1 year. Mantoux tests were done on all cases on admission, and, if negative, were repeated not sooner than eight weeks afterwards. All cases were followed up until there was no clinical or radiological evidence of respiratory disease; many were kept under observation for over a year, and one is still under observation almost three years after the onset of pertussis.

Criteria of Atelectasis

Complete collapse of an upper or lower lobe is often easy to detect clinically, though even here an infected atelectasis may be confused with pneumonic consolidation. Collapse of the right middle lobe, however, as Punch (1940) has pointed out, is usually completely masked by compensatory emphysema, and postero-anterior and lateral *x*-ray films are necessary for its detection. Doig (1946) and others have stressed that lordotic views often strikingly define atelectasis of the right middle lobe or lingular process.

When complete collapse of the right middle lobe can defy clinical recognition it is obvious that radiology is essential for the detection of small areas of atelectasis, and even then distinction from consolidation is not easy. If collapse is lobar or segmental in extent, postero-anterior and lateral *x*-ray films may reveal compensatory movements of the diaphragm, mediastinum, or interlobar fissures, and an opacity of characteristic shape, but when the collapse is very small these features are not seen. Diagnosis then depends on the appearance of the opacity and absence of pyrexia, leucocytosis, or other features of pneumonia, but, as infection and atelectasis may coexist, the distinction is often difficult. For this reason the diagnosis of small areas of atelectasis was not recorded unless confirmed by the independent opinion of a radiologist.

Radiological evidence of atelectasis was seen in 65 cases out of 150 (43%). The incidence in age groups is summarized in Table I.

TABLE I.—*Age Incidence of Atelectasis in 150 Cases of Pertussis*

Age in Years	Cases	Cases with Atelectasis
<1	44	9 (20%)
1—	30	14 (47%)
2—	19	11 (58%)
3—	17	9 (53%)
4—	13	8 (62%)
5—	12	8 (67%)
6—	11	6 (55%)
7—	3	—
8—	1	—
Total	150	65 (43%)

Lobar Incidence.—Some cases had more than one lobe involved, the lobes either showing atelectasis at the same time or becoming affected at different times. Thus, although atelectasis occurred in only 65 patients, more than 65 lobes were involved. In two cases the atelectasis was multilobular in distribution and these are excluded from the analysis. In the remaining 63 cases 85 lobes showed collapse of greater or less extent. Table II illustrates the number of times a particular lobe was involved, whether alone or in combination with other lobes. Table III indicates how often the lobes were affected singly and how often in combination.

TABLE II.—*Lobar Incidence of Atelectasis in 150 Cases of Pertussis*

Lobe	No. of Times Involved
Left lower	43 (50·5%)
Right lower	31 (36·5%)
Right middle	8 (9·4%)
Right upper	2 (2·4%)
Left upper	1 (1·2%)
Lingula	—
Total	85 (100%)

TABLE III.—*Anatomical Distribution of Atelectasis in 63 Cases of Pertussis*

Lobe or Lobes	No. of Times Involved
Left lower alone	25
Right lower alone	15
Left lower and right lower	14
Left lower and right middle	4
Right middle alone	2
Right upper alone	1
Right middle and right lower	1
Right lung and left upper	1
Total	63

Extent.—To indicate roughly the degree of lobar atelectasis encountered the collapse may be described as slight, moderate, or marked, the latter category indicating that the lobe was completely or almost completely collapsed, and

the other categories indicating lesser degrees of involvement. Of the 85 instances of atelectasis, 60 (70.6%) were slight, 15 (17.6%) moderate, and 10 (11.8%) severe.

Time of Onset.—Atelectasis affected 85 lobes, and the time of onset was as follows : first week of illness, 2 cases of lobar collapse ; second week, 10 ; third week, 18 ; fourth week, 24 ; fifth week, 12 ; sixth week, 8 ; seventh week, 4 ; eighth week, 4 ; ninth week, 1 ; tenth week, 1 ; eleventh week, 1. It will be seen that atelectasis occurred with increasing frequency until the fourth week of illness, and then its incidence declined.

Duration.—The duration in weeks of the collapse noted in the 85 affected lobes was as follows : 1 week, 16 instances ; 2 weeks, 12 ; 3 weeks, 20 ; 4 weeks, 16 ; 5 weeks, 9 ; 6 weeks, 3 ; 7 weeks, 3 ; 8 weeks, 3 ; 9 weeks, 1 ; 13 weeks, 1 ; 18 weeks, 1. It will be seen that atelectasis seldom lasted longer than five weeks. In general, it could be said that atelectasis of slight extent cleared up more quickly than that of marked degree, but there were exceptions to the rule. In one case, for example, in which there was complete collapse of the right lung and extensive collapse of the left upper lobe, complete re-expansion occurred in four weeks.

Bronchopneumonia in Relation to Atelectasis

Bronchopneumonia is an extremely serious complication of whooping-cough and is probably responsible for most of the deaths occurring early in the disease. It has been mentioned, however, that those patients who were admitted to hospital gravely ill and who died before radiological investigation was possible are not included in this series.

Bronchopneumonia was detected radiologically and clinically in 30 of 150 whooping-cough cases. Seven of them developed the condition after admission to hospital. Atelectasis occurred in 12 (40%) of these 30 cases with bronchopneumonia. In 120 cases *x*-ray evidence of bronchopneumonia was not found, and of these, 53 (44%) developed atelectasis. In this series, therefore, bronchopneumonia occurring in whooping-cough had no influence on the incidence of collapse. Bronchographic studies failed to reveal any evidence of bronchial dilatation in whooping-cough cases complicated by bronchopneumonia except in atelectatic areas, and follow-up clinical and radiological investigations did not demonstrate the development of bronchiectasis in bronchopneumonic cases.

Slight enlargement of hilar glands was demonstrated radiologically in 28 (18.7%) of the 150 whooping-cough cases, but in no instance could collapse be attributed to this condition.

Indications of Onset of Atelectasis.—When this study was begun it was believed that an elevation of temperature might prove a valuable indication that atelectasis had occurred. This expectation was not realized, for analysis of the cases failed to show any definite correlation between rise of temperature and the occurrence of atelectasis ; isolated temperature elevations were noted in cases in which collapse did not take place, while in some cases of extensive atelectasis the temperature was not elevated at all. It is interesting that Gray (1946) observed that pyrexia is less prominent when pulmonary collapse follows operations in the thorax than when it occurs after abdominal operations. None of the children complained of pain in the chest after pulmonary atelectasis, though some were too young to do so. Pleural friction was not detected over collapsed areas.

Conversion of the Mantoux test from negative to positive was not noted, nor did pertussis cause a "flare up" of existing foci of tuberculous infection.

Bronchial Dilatation in Atelectatic Areas of Lung

Six patients were encountered in whom pulmonary collapse of marked extent occurred. Two of them were under 1 year of age, and bronchography was not performed. This procedure was carried out in the four other cases, and in every instance well-marked dilatation of the bronchi in the collapsed area of lung was demonstrated. In one of these four cases there was extensive collapse of both lower lobes, with dilatation of the contained bronchi. Re-expansion of the right lower lobe took place after eight weeks, and re-expansion of the left lower lobe after nine weeks. Bronchography at this point showed very slight cylindrical dilatation of the bronchi in both lower lobes. Another bronchogram three months later showed that the bronchi had fully returned to their normal calibre. A "follow-up" examination showed no evidence of respiratory disease.

In the remaining three of these four cases the lung affected by the pulmonary collapse was relaxed by means of an artificial pneumothorax as a therapeutic measure. This must be mentioned, since the pneumothorax may have affected the duration of the atelectasis. In the first of these three cases the collapse affected the right middle lobe and the anterior basic segment of the right lower lobe. Re-expansion took place in eight weeks from the onset, and subsequent bronchography showed a normal bronchial tree. Eighteen months later a bronchogram revealed no abnormality and clinical observation did not show any evidence of pulmonary symptoms.

In the second of these cases the collapse affected the left lower lobe. Re-expansion occurred in thirteen weeks, and subsequent bronchography revealed a normal bronchial tree. A bronchogram eighteen months later again showed a normal bronchial tree, and there was no evidence of residual respiratory disease in a two-year "follow-up."

The third case had collapse of the left lower lobe on admission to hospital on March 26, 1947, and marked dilatation of the contained bronchi was subsequently demonstrated. The atelectatic area was grossly infected and the patient was gravely ill. Re-expansion took place eighteen weeks after onset, and subsequent bronchography showed an apparently normal bronchial tree. On discharge from hospital in September, 1947, the patient was free from symptoms, and physical and radiological examination of his chest revealed no abnormality. Since that time up to April, 1950, he has had three episodes of cough and sputum production lasting a fortnight or so during which crepitations could be detected over the left lower lobe. Bronchography on two occasions after his discharge from hospital revealed no definite bronchiectasis of the left lower lobe, though one set of films suggested slight cylindrical dilatation of the bronchi supplying the anterior basic segment. It seems probable that the left lower lobe bronchi have been damaged, though whether recovery will eventually take place remains to be seen.

Fifteen of the cases in the present series showed atelectasis of moderate extent, but the bronchi in the collapsed portion of lung were outlined in only 10. Of the 10 cases bronchographically investigated, bronchial dilatation was detected in four, but was very slight in extent. In all instances the collapse cleared up in approximately one month, and subsequent bronchography revealed a normal bronchial tree. A "follow-up" did not disclose any evidence of residual damage. Bronchography was also carried out in 10 cases in which atelectasis of slight extent was present, but bronchial dilatation was not seen.

For various reasons bronchographic examinations were performed on 25 of the whooping-cough patients in whom pulmonary collapse was not present. In some of these atelectasis had previously been detected and had cleared up, while others had suffered from the complication of bronchopneumonia. Bronchial dilatation was never demonstrated.

In this series of 150 cases of whooping-cough, therefore, three well-marked examples of "reversible bronchiectasis" were observed, and there was one case in which, though the collapsed area re-expanded and the dilated bronchi apparently reverted to normal, damage was sustained that may yet lead to progressive disease. In four other cases insignificant ephemeral bronchial dilatation was noted. Bronchial dilatation was never detected except in atelectatic areas.

Treatment

When pulmonary collapse is caused by aspiration of sputum into the peripheral parts of the bronchial tree postural drainage in the appropriate position (Nelson, 1934), or rolling the patient about and percussion over the affected area (Sante, 1927), may be employed in an attempt to dislodge the peccant mucous plugs. These methods were employed in the majority of cases and the collapse often cleared up, but it was difficult to evaluate their efficacy. Inhalation of carbon dioxide has been advocated for its effect in stimulating respiratory movements, and also for its reputed tendency to liquefy the mucous plugs (Coryllos, 1930; Brown, 1930; Banyai and Cadden, 1943). Bronchoscopic aspiration has also been employed, but in general has proved somewhat disappointing, for, although a mucous plug in a main bronchus may be easily removed, plugs in the peripheral bronchioles are obviously not so accessible. Blades and Dugan (1944), for example, had no success in four cases of collapse which subsequently resolved spontaneously, and Hennell (1946) failed in six cases, though he produced temporary re-expansion in one. Although desirable, this method was not employed in the present series.

It has been mentioned that in four cases in the series well-marked bronchial dilatation was demonstrated in collapsed lobes, and since the collapse was known to be recent it could be assumed that the bronchial dilatation was merely compensatory and likely to disappear if re-expansion of the lobe took place quickly enough. Pending re-expansion it was considered that, if the affected lung were relaxed by an artificial pneumothorax to an extent sufficient to counter the mechanical stresses dilating the bronchi, permanent bronchiectasis would be less likely to result. This measure was instituted in three cases, but, though the effect appeared to be favourable, no conclusions can be drawn.

Discussion

Engel (1947) has suggested that hilar adenitis is an important factor in the production of atelectasis in pertussis, and Paulson and Shaw (1949) have stressed that the right middle lobe bronchus is particularly likely to be compressed by enlarged hilar glands. Although slight enlargement of the hilar glands was noted in 18.7% of cases in the present series, collapse was never apparently due to this factor. In all instances of atelectasis the causative factor seemed to be obstruction of bronchioles or finer bronchi, and the likeliest mechanism aspiration of viscid sputum into the bronchial tree. At the same time it was often noted that a small area of atelectasis appeared which increased in extent over a period of two to three weeks, and if the cause were aspiration of sputum it would be anticipated that the collapse would be maximal from the beginning. Possibly in these cases the initial collapse was due to swelling of the bronchiolar mucosa or to aspiration of sputum with collapse of adjacent lung tissue due to subsequent "spill-over."

As Gray (1946) and others have pointed out that atelectasis occurs more often in children than in adults, possibly as a result of the narrower calibre of the bronchi, the low incidence of atelectasis in children under 1 year in the present series is interesting. Kohn *et al.* (1944) and Nicholson (1949) reported similar findings in pertussis, and it has been suggested that at this age little mucus is secreted by the bronchial mucosa.

Kohn *et al.* (1944) indicated that in pertussis a high incidence of right middle lobe collapse is to be expected, but in this series the incidence was that commonly found in respiratory affections, except for tuberculosis—namely, highest in the lower lobes, especially the left. In pulmonary tuberculosis Erwin (1939) found that collapse due to bronchiolar occlusion was most common in the upper lobes, and attributed this incidence to the fact that in tuberculosis secretion is found most commonly in this part of the lung. It is not easy, however, to apply this theory to pertussis. It is significant that the lobar incidence of bronchiectasis corresponds to the lobar incidence of atelectasis, and it is interesting that the lobar incidence of bronchiectasis in Tudor Edward's (1939) series of 166 lobectomies corresponds closely to the lobar incidence of collapse in this pertussis series, except that collapse of the lingula was not noted in the present study, though carefully looked for.

The comparatively frequent occurrence of "reversible" bronchiectasis was noteworthy, for, although the condition has been recorded by Findlay and Graham (1931), Findlay (1935), Jennings (1937), Franklin (1938), Raia (1938), Wilson (1939), Fleishner (1941), Ogilvie (1941), Diamond and Van Loon (1942), Blades and Dugan (1944), Lander (1946), and Wearing (1948), it is still regarded as something of a rarity, though it is probably observed much more commonly than reported. Lisa and Rosenblatt (1943) and Hinshaw and Schmidt (1944) denied that it was bronchiectasis at all, and thought the appearance of dilatation was an illusion due to foreshortening and crowding of the bronchi, but, as Ogilvie (1941) and Lander (1946) reported cases in which the collapse cleared up and the affected bronchi remained dilated, little doubt can now be entertained that the bronchi may be mechanically dilated as a result of pulmonary collapse, and that supervening infection may render the dilatation permanent.

How long atelectatic bronchiectasis may remain potentially reversible is unknown. In many of the reported cases the duration of the collapse could not be ascertained with certainty, but in one of Lander's (1946) cases the collapse lasted for four months, in Wearing's (1948) case it lasted for at least four months, and in a case reported by Raia (1938) the duration seems to have been six months. The degree of infection is doubtless the main factor militating against recovery, but it is conceivable that mere prolonged mechanical distension might leave the bronchi dilated even if the collapse cleared up, though this would possibly not be of much importance.

It was anticipated that small areas of collapse would not give rise to bronchial dilatation, as compensatory emphysema would be sufficient to relieve strain on the bronchi, and, as has been noted above, this expectation was realized in practice.

The incidence of respiratory disease following pertussis in this series was very low. Pulmonary collapse was noted in 43% of the patients, but in general it was small in extent

and ephemeral. Re-expansion took place in all instances before the patient was discharged from hospital, and in only one case did prolonged clinical and radiological follow-up reveal residual damage to the respiratory tract, and even here eventual recovery seems to be possible. Kohn *et al.* (1944), in a clinical and radiological study of 222 cases of pertussis, did not mention any sequelae, but Nicholson (1949) reported 22 cases of collapse of more than two months' duration in a series of 48 pertussis patients, and stated that in seven followed for a year the collapse was still present.

Whatever the general incidence of pulmonary collapse in pertussis, its importance is obvious, for its relationship to bronchiectasis seems clear. As in many cases it is impossible to detect atelectasis clinically, an *x*-ray film before supervision ceases would seem to be the minimum demand on the radiological department. If, however, respiratory symptoms follow pertussis it cannot be too strongly emphasized that a negative *x*-ray film is of little significance, for atelectasis may have cleared up, leaving bronchiectasis behind. It still does not appear to be widely appreciated that recurrent attacks of cough or "pneumonia" and persistent localized crepitations call for bronchography; even to-day there is a tendency to wait for the appearance of copious sputum and clubbing of the fingers before suspecting bronchiectasis.

If atelectasis is detected during or after the attack of pertussis every effort should be made to promote re-expansion of the affected lung, remembering that this has happened six months after the onset of atelectasis (Raia, 1938), and may perhaps occur even up to a year afterwards. In general, surgical removal of a lobe collapsed for less than a year would appear to be inadvisable. When bronchial dilatation remains after re-expansion of a collapsed lobe it is no longer merely compensatory, and so far as is known will be permanent.

Where bronchial dilatation is pronounced, and evidence of infection obvious, surgical intervention is the treatment of choice, for the prognosis in such cases treated medically, as judged by the work of Findlay and Graham (1927), Roles and Todd (1933), Ford (1948), and others, is poor, though antibiotics and chemotherapy can nowadays generally cope with acute exacerbations. On the other hand, it may safely be said that the prognosis of cases with mild bronchial dilatation and little evidence of infection cannot be stated with any confidence, and a prolonged period of observation before advising lobectomy would appear to be indicated.

Summary

Atelectasis was noted radiologically in 43% of 150 pertussis cases, but in general it was slight in extent and of comparatively short duration. Six instances of virtually complete lobar collapse took longer than two months to resolve; in five of these the bronchi contained in the collapsed lobes were shown to be dilated and were seen to revert to their normal calibre when the lobes re-expanded. In the remaining case bronchography was not performed.

In four partially collapsed lobes slight bronchial dilatation was noted, which disappeared when the collapsed lung re-expanded.

In only one case did the attack of pertussis lead to persistent respiratory symptoms. In this case there was evidence of residual bronchial infection in a lobe which had been atelectatic for eighteen weeks. Although the bronchi in this lobe were markedly dilated when it was collapsed, bronchiectasis was not obvious after re-expansion.

The treatment of atelectatic bronchiectasis in pertussis is discussed, and a trial of artificial pneumothorax mentioned.

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SOME ASPECTS OF COLOUR-BLINDNESS*

BY

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In spite of the existence of numerous tests for colour-blindness, each to some extent based on one of the various theories of colour-vision and largely directed to the selection of personnel for the armed Forces and for certain branches of industry, there is no single test which can be regarded as infallible. This fact perhaps reflects more than anything else the inadequacy of colour-vision theories and the insecure basis upon which most of them rest. The occasion is thus opportune for a review of some of the fundamental aspects of the problem and for an evaluation of certain recent observations on colour-blind subjects.

Ever since the days of Thomas Young the necessity for three variables in the mechanism for normal colour-vision has been recognized, and three separately excited pathways from the eye to the brain have been postulated. More than three such pathways are usually considered unnecessary, though at times more have been suggested in order to account for special aspects of colour-vision. Perhaps because of the common experience of mixing pigments, and among physicists and physiologists of mixing lights, in which three primary colours are required in order to match all the spectral colours, it has generally been assumed that each pathway registers the sensation of one of the primary

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colours—that is, there is a blue pathway, a green pathway, and a red pathway. Each pathway, when stimulated alone, would then give rise to the sensation appropriate to it. When two or more pathways were stimulated, intermediate hues would be obtained—for example, yellow, blue-green, etc. This idea has commonly been elaborated further to suggest that the actual receptor cells in the retina must be of three classes—red receptors, green receptors, and blue or violet receptors.

While the triploid character of normal colour-vision can hardly now be doubted, this somewhat naive conception of the complex mechanism involved must be regarded as inadequate, and the position must be examined afresh.

Activation of the Retinal Receptors

From the information which is available on the behaviour of one class of retinal receptors—namely, the rods and their contained rhodopsin or visual purple—and if it is assumed that the other receptors behave in a similar manner, it seems probable that the retinal receptors in general may be activated by substances with relatively broad absorption spectra, so that they are sensitive to a wide range of wavelengths. This is borne out also when the spectral sensitivities of eyes possessing predominantly cones are considered.

On the other hand, some recent work on the properties of certain photosensitive substances produced in the laboratory by the breakdown of visual purple may indicate the possibility of active substances with much narrower absorption bands and therefore with greater selectivity; but so far there is no direct evidence that these substances occur under physiological conditions. The sensitivity of the rods lies mostly between 400 mμ and about 640 mμ, with its maximum at about 500 mμ. Eyes dependent on cones, on the other hand, have a range extending from 440 to 700 mμ, with maximum sensitivity at about 570 mμ. It is well known that when the rods are responding alone, as they may do in very dim light, they give rise to a colourless sensation. The eye under such conditions cannot discriminate between wavelength and intensity. A given frequency of nerve impulses in the optic nerve fibres may be initiated by the appropriate intensity of any wavelength. This observation is also likely to be true for any other single group of receptors so long as they are responding alone, whether they be rods or cones, and whatever the nature of the photochemical activator.

When, however, a second group of receptors, whose spectral sensitivity differs from that of the first group, responds simultaneously, it is at least theoretically possible for differences in wavelength to be appreciated as well as differences in intensity provided that the information obtained from the two sources is not completely "pooled" before reaching the centre in the brain where colour sensations originate. The following observation indeed seems to indicate that this can apply to the rods and the cones as the two groups with different spectral sensitivities.

If one-half of an observation field subtending about 4 degrees at the eye is illuminated with light of any wavelength between yellow and violet, but of such a low intensity that the colour is indistinguishable to a well dark-adapted eye, it is generally believed that the rods alone are being stimulated and that the light is below "cone threshold." Nevertheless it is found that at these very low intensities, if the other half of the field is illuminated by a yellow, orange, or red light of just enough strength to evoke a colour sensation from this half, it also evokes a blue sensation from the other half. The blue disappears if the stimulus to the rods is removed by turning off the original light. The rods must clearly contribute to this sensation of blueness, and the particular blue which they induce can, by binocular matching, be found to give rise to the same sensation as a spectral band between 460 mμ and 470 mμ. This experiment is most easily interpreted as indicating that the rods give rise to a colourless sensation when functioning alone, but are concerned in the perception of blue when responding in juxtaposition to active cones—that is, under conditions when a comparison between two separately stimulated pathways is possible. It does not exclude the possibility that there are other conditions of stimulation in the eye which the brain interprets as blue.

An eye which has no hue discrimination, as distinct from brightness discrimination, and which has only one group of receptors or one pathway to the colour centre, is described as monodic and the resulting vision is monochromatic or achromatic.

If there are two types of receptor and two pathways differing in spectral sensitivity the eye is diodic, and though some colour-vision is certainly possible it will be dichromatic in character and thus defective as compared with that of the normal subject. It will be possible to match all the spectral colours by mixtures of only two primaries, if these are suitably chosen. Conversely, if it is possible for an eye to match all spectral colours by mixtures of red and violet then its visual mechanism is diodic (or monodic) and it is unlikely to have more than two independent pathways, or at least the information received by the brain must be treated as arriving through two separate pathways only.

A Third Factor

In order to prevent the confusions characteristic of the diodic system, some third factor must be present in the normal eye. This may take the form of a third receptor and pathway whose spectral sensitivity is different from those of the other two, or it might take the form of a local modification of one of the existing receptors, or even of both, in such a way that the spectral sensitivities are altered in a particular area of the retina and the nerves from this particular area are separately connected to the brain. Such a situation might be brought about by screening some of the receptors, as, for example, behind macular pigment. Alternatively, the products of the breakdown of their own photosensitive pigments may act as colour filters for certain receptors—for example, the rods might be screened in daylight by a filter of the yellow breakdown products of rhodopsin. It is not necessary, therefore, to assume as an absolute essential the existence of three morphologically distinct groups of receptors provided that there is some mechanism by which three pathways, or separate groups of nerve fibres, receive stimuli which are different from each other at least in those parts of the spectrum in which vision is trichromatic in character.

Moreover, owing to the connexions and cross-connexions which bring about both summation and inhibition in the retina, the actual responses in the pathways may bear very little resemblance in the frequencies of their nerve impulses to the frequencies which might be expected from the sensitivities of the actual photosensitive receptors. An eye, for example, which depended on only two primary receptors might have at least five sets of nerve fibres each transmitting a different frequency of impulses. Fibre 1 might send impulses corresponding to the spectral sensitivity of receptor A, fibre 2 impulses corresponding to the spectral sensitivity of receptor B; on fibre 3 impulses from A might be inhibited by those from B; on fibre 4 those from A

might antagonize those from B; and on fibre 5 impulses from A and B might summate. Each of these fibres, and an endless series of others relaying other combinations of response, would probably show a different spectral sensitivity of response from all the others, but, since the fibres are not independently stimulated and depend only on recombinations from the two primary receptors, such an eye would be essentially diodic or dichromatic and would be able to match all spectral colours by means of two primaries only.

It is important to remember at this point that all the nerve impulses which have been recorded from the eyes of vertebrates have been recorded from fibres in which there is every likelihood of such combinations having already occurred in the retinal synapses. It is therefore very dangerous to attempt to correlate directly the spectral sensitivities of such pathways with the spectral sensitivities of the primary receptors, except in the relatively simple case of those dependent only on the known pigment, rhodopsin. More subtle methods have to be used to work back from the impulses recorded to the receptors stimulated.

The Trichromatic System

When the eye is treated as a whole—that is, when relatively large fields are used for the investigation of colour—any spatial differences of activity in the retina tend to be eliminated, and under these conditions the normal eye is definitely a triodic or trichromatic system. It is therefore necessary, in exploring colour-vision, to seek either for three independent receptors or for two main receptors and, in addition, for another factor which will modify the activity of some of these receptors in such a way that they may act as a separate group.

This trichromatic character of normal colour-vision, however, vanishes when vision is restricted to small fields in certain areas of the retina and when the intensity of the light used in the small fields is not so high that the stimulus spreads to neighbouring regions. Under these conditions the extreme periphery of the eye in most subjects is achromatic or monodic. Only light is perceived in this zone, and there is no sensation of colour. A zone rather less far out in the periphery is diodic, and in this zone all spectral colours can be matched with mixtures of two primaries. In the blue-green region of the spectrum there is a colourless or neutral point, and on either side of this point sensations are aroused of blue on one side and of yellow on the other. Thirdly, there is a region in the very centre of the fovea, at the point where form vision reaches its maximum precision, where another form of dichromasy occurs. Spectral colours when flashed momentarily on this area at very low intensity are seen in terms of blue-green, colourless, or orange; with "continuous" vision, yellow is matched with white and all spectral colours can be matched with mixtures of red and violet; at threshold levels, only red and violet remain coloured, all other colours appearing grey at the threshold. Provided that the fields are small enough and are held still enough on the eye, this form of dichromasy may occur elsewhere on the eye also, but it has been less fully investigated under such conditions. The reduced colour-vision which occurs in dim light is also not unlike this type.

Main Types of Colour-blindness

It is pertinent now to ask how these forms of local dichromasy or partial colour-blindness in the normal eye compare with those occurring naturally in colour-blind subjects. Secondly, how are they related to retinal structure? And, thirdly, how do the various types of colour-blind subjects behave under similar conditions? To these questions only very partial answers can at present be given, the chief reason for this being that there are many types of colour-blindness and there is as yet no histological evidence regarding any peculiarities in their retinal structure. Nevertheless, some progress can be made, and the approach will become clearer if the main types of colour-blindness are first briefly reviewed.

Colour-blind subjects can be divided into three main groups, each of which has several subdivisions.

Achromats or Monochromats.—These have no colour sense whatever and can match any colour with any other colour provided that the intensities are equalized. Some of these are maximally sensitive in the green region of the spectrum at about 500 mμ; a second group are most sensitive at 540 mμ, and a third group between 560 and 570 mμ. Once again it must be emphasized that monochromasy does not necessarily imply only one type of receptor. It may arise even if three or more receptors are present and the information which they provide is pooled before reaching the brain—that is, if there are not separate pathways each capable of being stimulated somewhat selectively by the various receptors. It is not known, therefore, whether these maxima represent those of three different types of receptor or result from some combination of receptors. The maximum at 500 mμ is thought to indicate the presence of rods only, and it is interesting to note that such subjects, though they may be photophobic, are not blind in daylight.

Dichromats.—These are able to match all the colours of the spectrum with mixtures of red and violet, and they may be divided into at least three clear groups. There are the protanopes (sometimes called red-blind), who have low sensitivity to the red end of the spectrum and are most sensitive at 540 mμ. They match a point in the blue-green region (about 490 mμ) with white. Secondly, there are the deuteranopes, and these form a more heterogeneous group. On the one hand the spectral sensitivity curve may not differ from that of the normal subject, and on the other it may have its maximum displaced towards the red end of the spectrum to about 575 mμ. The neutral point—that is, the point in the spectrum which can be matched with white—varies between 500 mμ and 520 mμ. Both these types of colour-blindness are congenital.

Tritanopes.—These are much rarer, and very often, if not always, tritanopia results from pathological changes in the eye. It is characterized by a neutral point at 570 mμ and generally a low sensitivity to blue and violet, though the maximum sensitivity is within the normal range.

In each of these groups the subjects habitually make certain well-defined colour confusions, and indeed it is upon these confusions that many established tests for colour-blindness depend. Protanopes and deuteranopes can match red with green on a 2-degree field. In general they seem to separate colours into blues, corresponding to wavelengths between violet and the neutral point, and yellows from the neutral point to the red end of the spectrum, and it is interesting to note that the maxima of their sensitivity curves correspond rather closely to the maxima of those found in the monochromats.

There is another group of subjects who cannot match all the spectral colours by means of only two primaries—that is, they are trichromats, but in making matches of yellow, for example, with mixtures of red and green, they require different proportions of these colours from those required by normal people. Probably the majority of these "anomalous trichromats" have some degree of true colour-blindness—that is, they are tending towards protanopia, deuteranopia, or tritanopia, but are not sufficiently abnormal to be able to dispense with the third primary altogether.

Finally, when the Ishihara plates are used as a test for colour-blindness, some individuals are found who would be diagnosed as red-green blind—that is, as either protanopes

or deuteranopes—but on further testing they are able to distinguish all the spectral colours correctly and cannot match red with green or even with yellow on a 2-degree field. These subjects apparently associate colour in a different way, and there is some instability in their colour sensations. For example, an orange field may be correctly named if standing by itself, but will be called green if placed next to a red, or red if next to a green field. On the Ishihara plates the various spots are recognized as different and are often correctly named, but they may be grouped quite differently from the way in which they are grouped by normal subjects. Consequently the plates are read incorrectly or not at all, but for a quite different reason.

Normal Vision and Colour-blindness Compared

The behaviour of normal subjects when different parts of their retina are investigated by means of small fields may now be compared with that of colour-blind subjects both when using the whole eye and also when their vision is similarly restricted. The dichromatic zone in the periphery at about 60–70 degrees from the optic axis exhibits a type of deuteranopia. Its neutral point lies in the blue-green or green region of the spectrum, and there is no evidence of any markedly decreased sensitivity to red as compared with green when the eye is maintained in a steady light-adapted condition.

Structurally the retina is much simpler in this region than it is towards the centre, and attention may be called to the limited number of ganglion cells and thus to the limited number of separate pathways to the brain from this area. A detailed analysis of these ganglion cells and their connexions would probably prove of great interest. There are certainly two main histologically distinguishable classes. Some very large cells with well-defined Nissl's granules are interspersed among numerous much smaller cells with less-granulated Nissl's substance. In the extreme periphery the ganglion cells are still less abundant while the receptors themselves are not much reduced, so the achromasy of this zone probably results from the paucity of optic-nerve fibres. These peripheral regions of the eye in all probability represent parts which have not evolved so far as the more central regions, and may therefore offer clues concerning the evolution of the colour-vision mechanism.

In contrast to the deuteranopia of the peripheral zone, the foveal centre of the normal subject behaves as a tritanopic system and makes the confusions characteristic of this type of dichromasy. Its neutral point is in the region of 570 mμ. It thus behaves as if it possessed only two pathways and as if the pathway sensitive mainly in the violet region of the spectrum was absent or physiologically inactivated.

Foveal Centre of Those who are Red-green Blind

If the foveal centre is investigated in the same way in those dichromats who are red-green blind—the protanopes and the deuteranopes—it is found then to be completely colour-blind or monochromatic. That is to say, when the field of vision of the protanopes and deuteranopes is confined to the foveal centre all sense of colour goes and any spectral colour can be matched with any other when there is equality of brightness. The area behaves as if one pathway alone was functional. In the protanopes this pathway has its maximum sensitivity at 540 mμ. In the deuteranopes the most sensitive region ranges between 555 mμ and 580 mμ, of which the former does not differ from that of the normal observer.

When the deuteranopes are investigated further the possible meaning of this divergence becomes clear. If, for simplicity, it is assumed that the normal eye has three receptors, R, G, and B, so lettered as to indicate the region of the spectrum (red, green, or blue) in which they are most sensitive, then the foveal centre behaves as though B were absent or suppressed, thus leaving only R and G functional. Now red-green dichromats might be expected to have reduction of the R receptor (protanopes) or of G, or they might well possess both R and G receptors but have no differentiation of the pathways arising from them. The foveal centre of the red-green blind might therefore have a sensitivity corresponding to R, to G, or to R + G. By adapting or fatiguing the eye to selected wavelengths it should be possible, by studying the effects of such adaptation on the ensuing sensitivity, to decide whether the foveal centre of dichromats contains one or two types of receptor.

A study of some twenty deuteranopes in this way has given a very clear indication that they tend to be divisible into two classes. In the first class, the spectral sensitivity is normal and the effects of selective adaptation are identical with those found in the normal subject. Since, however, these dichromatic subjects are monochromatic in the central fovea, they presumably have receptors R and G, but their effects must be combined on to one pathway—that is, they behave as R + G. At the other extreme, five subjects have been investigated in whom there is no selective adaptation. In them it is immaterial what wavelength is used for the adapting light; the thresholds for violet, or blue, and red are always raised equally by adapting lights of equal subjective brightness. These subjects have their maximum sensitivity at about 575 mμ and probably possess receptors of the R type only, so their spectral sensitivity curve probably represents the spectral sensitivity of the R receptor of the normal eye. The shape of this sensitivity curve is very similar to that of the visual purple absorption spectrum, but the curve is shifted towards the red. Moreover, it is of special interest to find that the sensation which these subjects record from the foveal centre is "colourless," just like the sensation aroused by rods only, but it becomes coloured when comparisons are possible. Between these two extremes there are other deuteranopes who show intermediate stages with regard both to the adaptation effects and to the position of the luminosity curves.

Insufficient protanopes have so far been examined by the method of selective adaptation to say whether the maximum sensitivity of their fovea at 540 mμ corresponds to the action of the G receptor only or whether more than one receptor enters into the formation of this pathway. The first experiments indicated that perhaps two receptors were involved, but later experiments throw some doubt on this interpretation, and the point is not yet settled.

Once again, detailed examination of the structure of the foveal centre, not only with regard to the receptors but also with reference to the bipolar cells, ganglion cells, and their central connexions through the lateral geniculate body, is required in order to establish the nature of these pathways. There are, for example, some indications that the very large ganglion cells of the periphery are not present among those connecting with the central foveal elements. The "mop" bipolar cell, which relays mostly from rods, is also scarce in or absent from this area. Moreover, there are indications of at least two types of cone in the foveal centre of monkeys, and the participation of rods, among which histology reveals two separable groups in monkeys and frogs, cannot now be so confidently excluded from daylight vision as was done by earlier investigators. In fact, one of the

main problems in vision to-day is the question of what the rods are doing under photopic conditions.

Conclusion

Enough has been said to indicate that the rigid trichromatic theory and the dogmatic assertion of the presence of three types of cone in the fovea of the normal eye are not entirely satisfactory. The study of specific retinal areas, functionally by the use of small fields, structurally by the use of reliable histological methods, and electrophysiologically in other animals, is now the obvious method of approach. Further work on the same lines with colour-blind subjects can almost be guaranteed to yield further dividends. In particular, a more enlightened approach to the evolution of visual mechanisms may well give clues on the nature of the mechanism for colour-vision : thus, there are many indications that the colour-sense may have arisen when a central apparatus was evolved for comparing and evaluating the information already reaching the brain through separate channels previously developed for other purposes—for example, for night and day vision, for increased visual acuity, etc. The time has now come, therefore, for a more biological and comparative approach to the subject. The working of the human eye cannot be treated in isolation as a purely physical or psychological problem ; it must be studied in relation to the evolutionary history of vision as a whole.

INFLUENCE OF ASCORBIC ACID ON THE HEALING OF CORNEAL ULCERS IN MAN

BY

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It is accepted that the repair of collagenous tissue is dependent on an adequate supply of ascorbic acid (Höjer, 1924 ; Menkin, Wolbach, and Menkin, 1934 ; Wolbach and Howe, 1926). Furthermore, ascorbic acid has been shown by Schmid and Bürki (1943), Henkes (1946), and Pirie (1946) to exist in a relatively high concentration in the cornea. The cornea is largely composed of collagen. It is, moreover, avascular. Thus vitamin C may play an unusually important part in the metabolism of this special tissue and possibly also in the resolution of corneal lesions.

Galloway, Garry, and Hitchin (1948), working with guinea-pigs, found that the healing of superficial injuries made with a dental burr and involving only the epithelium was not delayed even when the guinea-pigs were in a subscorbutic state. In their experiments, however, healing may have been effected predominantly by a sliding of epithelial cells from the corneal margin (Arey and Covode, 1943 ; Buschke, Friedenwald, and Fleischmann, 1943 ; Mann, 1944). In such injuries there was no occasion for new formation of collagen.

Campbell, Ferguson, and Garry (1950), using heat injuries to the epithelium alone in scorbutic guinea-pigs, confirmed the findings of Galloway, Garry, and Hitchin (1948) ; but they showed that deeper burns, involving the anterior two-thirds of the corneal stroma, took approximately 30% longer to heal in scorbutic guinea-pigs than in those fully saturated with ascorbic acid. Furthermore, even after epithelial healing was complete, structural weakness of the wound persisted for as long as three weeks after the injury in the scorbutic animals, while in the saturated guinea-pigs the strength of the cornea was restored in 11 days.

These results suggest that ascorbic acid may be of value in the treatment of human corneal lesions. In order to test this possibility we undertook the present investigation. Our study was restricted to the healing of small corneal ulcers in man so as to simulate the animal experiments conducted by Campbell, Ferguson, and Garry (1950). Suitable cases can readily be collected in sufficient numbers to justify statistical analysis.

Such an investigation on human beings can never hope to be so clear-cut as that on the guinea-pigs, in which the experimental group was reduced to a subscorbutic state and the control group had an ample intake of vitamin C. All our patients were eating a more or less normal diet, the intake of vitamin C probably reaching 50 mg. daily in some cases. Therefore, in order to produce blood levels in sufficient contrast with the group on a normal diet, we gave half our patients very massive doses of vitamin C.

Method

The patients studied in this investigation were in attendance at the out-patient department of the Glasgow Eye Infirmary between November, 1949, and March, 1950.

Approximately half the patients received 0.5 g. of ascorbic acid three times daily ; the remaining patients received control tablets containing no ascorbic acid, but of identical appearance and taste. Thus the patients in the principal group probably received 30 to 50 times as much ascorbic acid as the patients in the control group, who received ascorbic acid only in their diet. Administration was continued until healing was complete.

The clinical examination of the patients was carried out by one of us (T. A. S. B.), who throughout the experiment was unaware of the type of tablet administered to each patient.

A detailed clinical history was obtained from each patient. This was followed by a careful examination of the lesion, and such details as its size and position on the cornea were noted.

To assess the extent of the ulcer one drop of a 2% aqueous solution of sodium fluorescein was instilled into the conjunctival sac. After one minute exactly, excess fluorescein was washed off with a stream of isotonic sodium chloride solution delivered from a pipette. The intensity of fluorescence of the ulcer was then measured in a dark room by placing alongside the patient's eye a series of standard strips of filter paper impregnated with varying concentrations of sodium fluorescein. Fluorescence was induced by exposure to a mercury vapour lamp fitted with a Wood's glass screen, and situated about 2 feet (60 cm.) from the patient.

Our standard consisted of five strips, 1 by ¼ in. (2.5 by 1.25 cm.), of No. 1 Whatman filter paper impregnated with fluorescein so that the intensity of fluorescence increased in approximately linear steps (Campbell and Boyd, 1950). Table I gives details of these standard strips.

As healing of a corneal ulcer progresses, the intensity of the fluorescence decreases and finally ceases when epithelization is complete. The time of healing was recorded as the interval between the first examination of the ulcer and the cessation of fluorescence. Observations were carried out daily.

TABLE I.—*Relation of the Concentration of Sodium Fluorescein to the Intensity of Fluorescence from the Standard Strips of Filter Paper for Clinical Use*

Intensity of Fluorescence	Concentration of Fluorescein in μg/cm.² of Filter Paper
0	No fluorescein
1	0·5
2	1
3	2
4	4
5	8

Before the patient's final discharge the cornea was examined by slit-lamp and biomicroscope. The depth of the lesion was assessed by measuring the fraction of the thickness of the cornea now occupied by opacity.

Results

Analysis of the time taken for the corneal ulcers to epithelize showed that the mean healing time for the group of patients who had received ascorbic acid (22 cases) was 4 days, whereas for the control group (29 cases) the mean was 4.82 days. The difference, 0.82 days, is not significant. However, several factors which may have affected these times of healing were at work simultaneously. We therefore broke down our groups under the following headings.

1. Depth

The two groups above were further divided into subgroups of patients with "superficial" and with "deep" ulcers. Ulcers were considered to be "superficial" if, after healing, the residual opacity occupied a quarter or less of the corneal thickness as judged by slit-lamp and biomicroscope. The remainder were considered to be "deep."

Under normal circumstances one expects superficial ulcers to heal more rapidly than deep ulcers. This was indeed the case in the control group, in which the difference in healing time was highly significant (Table II, B D) ($P<0.0001$).

TABLE II.—*Relationship of Mean Healing Time to Depth of Corneal Ulcers*

Depth of Infiltration	Mean Healing Time in Days: Principals (Receiving 1·5 g. Additional Ascorbic Acid Daily)	No. of Cases	Controls (No Additional Ascorbic Acid)	No. of Cases
Superficial ..	A 3·63 (±0·54*) C	11	B 3·80 (±0·50) D	15
Deep	4·36 (±0·40)	11	6·15 (±0·50)	13

* Standard error of mean.

In the group of patients receiving 1.5 g. of ascorbic acid daily the superficial ulcers also healed more rapidly than the deep ulcers, but this difference was not significant (Table II, A C). In other words, there is a suggestion here that depth of lesion has less effect upon the healing time when there is an abundant intake of ascorbic acid.

2. Ascorbic Acid

The difference between the mean healing times of the groups of patients with and without additional ascorbic acid is not significant in the case of superficial lesions (Table II, A B), but is significant in the case of deep lesions (Table II, C D) ($P<0.05$). This means that there is evidence that the administration of large doses of ascorbic acid does not influence the rate of healing of superficial ulcers, but that it does accelerate the healing of deep ulcers.

The significant difference between the time necessary for epithelization of "deep" ulcers in the principal and control groups is further substantiated by an examination of the course of healing in these two groups. Information on the course of healing was derived from daily estimation of the degree of fluorescence from each ulcer. In Fig. 1 the mean intensity of fluorescence on each day of observation has been plotted for the "deep" ulcers in the principal and control groups. Although by chance the group receiving ascorbic acid started with a higher degree of fluorescence, epithelial healing occurred rapidly, and so their "fluorescence gradient" was much steeper than that of the controls. In contrast, the "superficial" ulcers in principal and in control groups healed at similar rates (Fig. 2).

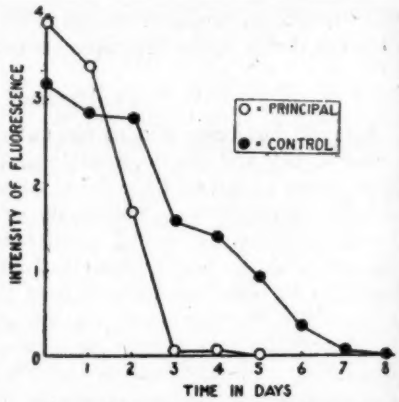

FIG. 1.—Mean intensity of fluorescence of deep corneal ulcers treated with (principals) and without ascorbic acid (controls) plotted for each day during healing. The figures on the ordinate correspond to the strip intensities described in the text.

It is thus clear that the course and time of healing were appreciably influenced by ascorbic acid only in deep ulcers; but can it be said that the deeper the lesion the more pronounced is the effect of ascorbic acid?

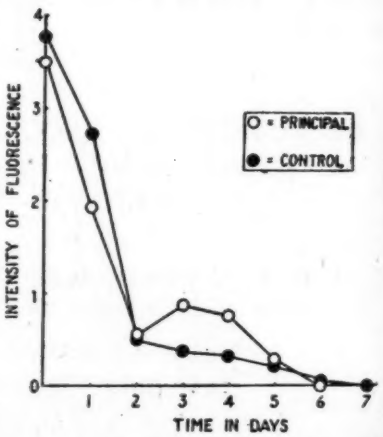

FIG. 2.—Mean intensity of fluorescence of superficial corneal ulcers treated with (principals) and without ascorbic acid (controls) plotted for each day during healing. The figures on the ordinate correspond to the strip intensities described in the text.

This question was investigated by a further subdivision of the deep and superficial groups. The deep group was broken down into a group in which the ulcers infiltrated one-half of the corneal thickness and another group affecting one-third. Similarly, the superficial group was divided into groups affecting one-quarter and one-fifth.

Fig. 3 shows diagrammatically the mean healing time of principals and controls in each of the four groups. The influence of depth upon the control groups is clearly shown by the progressive lengthening of healing time with increase of depth. There is a similar influence at work in the

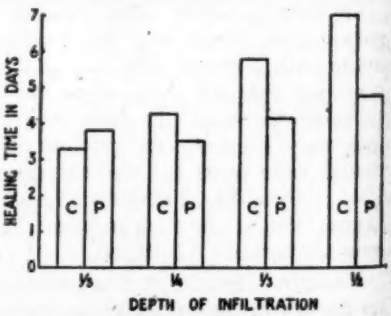

FIG. 3.—Mean healing time related to depth of infiltration in corneal ulcers treated with (P) and without ascorbic acid (C).

principal groups, but it is much less marked. It can thus be said that the deeper the lesion the more pronounced is the effect of ascorbic acid.

3. Site and Size

A priori, one might expect the area of the ulcers and their location on the cornea to have some effect on the rate of healing. We found only a slight tendency for central ulcers to heal more slowly than marginal ones, but analysis indicated that this difference could easily have arisen by chance.

As one would expect, the larger ulcers healed more slowly than the smaller ones, but the difference between the healing times of large and small ulcers in the series we examined was not significant. This was probably due to the comparatively small size of the ulcer diameters (0.25 to 2.5 mm.) in the cases included in this survey.

4. Local Therapy

All the cases received either gutt. sodium sulphacetamide 10% or gutt. penicillin 1,000 units per ml., three times daily; it was found that there was no significant difference between the healing times of sulphacetamide- and penicillin-treated cases. It is of interest, however, to note that, compared with sulphacetamide, penicillin significantly shortened the duration of conjunctival discharge.

5. Pyorrhoea

During the routine examination of our patients we noticed that a considerable number had pyorrhoea, and so decided to investigate its incidence. Pyorrhoea was said to be present only if the gums showed marked retraction with ulceration, or if pus could be expressed from the parodontal sulci.

Pyorrhoea occurred in these patients with corneal ulcers most frequently in the 20–40-year age group. Younger patients were usually free from infection, while many of the teeth of the older patients had been extracted. Since age appeared to affect the incidence of pyorrhoea, we collected a control group with the same age distribution from out-patients attending with non-infective ocular complaints and examined them for the presence of pyorrhoea.

Pyorrhoea was more common in the group with corneal ulceration (Table III). The χ^2 test showed that this difference in incidence was significant ($P<0.01$).

TABLE III.—*Incidence of Pyorrhoea in Patients Suffering from Corneal Ulcers Compared with a Control Group with Non-infective Eye Conditions*

	No. of Patients With Pyorrhoea	No. of Patients Without Pyorrhoea
Patients with ulcers	20 (69%)	9 (31%)
Patients without ulcers (control group)	8 (28%)	21 (72%)

$\chi^2 = 8{\cdot}4$. $P<0{\cdot}01$.

Discussion

Superficial Lesions of the Cornea

The absence of a significant effect of large doses of ascorbic acid on the healing times of superficial ulcers is in keeping with the results of Galloway, Garry, and Hitchin (1948), who inflicted mechanical wounds on the corneal epithelium, and of Campbell, Ferguson, and Garry (1950), who used thermal injuries. These workers considered that ascorbic acid is not required for a purely epithelial repair. The ulcers classified as superficial in the present series were not confined to the epithelium, but did involve a certain amount of stroma. The effect of this involvement of stroma on healing time appears to be masked in the superficial group. However, it becomes apparent when deep lesions are considered.

Deep Lesions of the Cornea

Large doses of ascorbic acid in man, however they act, do promote epithelization of deep corneal ulcers as judged by our fluorescein test. It may be that the slower rate of epithelization in the deep ulcers, where no addition of ascorbic acid had been given, was due to the absence of a suitable substratum of collagenous tissue. This is in keeping with the hypothesis of Hartwell (1929), who studied skin epithelization in cases of scurvy. This is not to say that there must be complete filling of the crater of the ulcer with collagenous tissue before the epithelium can spread across.

We can only conclude that in the patients receiving very large doses of ascorbic acid some changes had taken place in the exposed collagen of the bed of the ulcer to permit rapid overgrowth of the epithelium.

Action of Ascorbic Acid

The question now arises: "Why should massive doses of ascorbic acid accelerate the healing of corneal lesions in patients whose vitamin-C intake seemed normal?" We would like to stress that after careful questioning on dietary habits we found that there were very few patients who did not eat potatoes and vegetables daily. As no patient showed signs of scurvy it seems that this intake was sufficient for normal purposes, but our findings suggest that it was not optimum for the healing of corneal lesions. We therefore suggest that ascorbic acid, in such massive doses as 1.5 g. daily, has a value in therapy apart from its normal role as a vitamin at accepted levels of intake.

The nature of this action remains obscure at present. It may well be that there is a local deficiency at the site of any collagenous tissue lesion. If this be so, then benefit would accrue from the increased rate of diffusion which would arise from a temporary increase in the blood level of ascorbic acid. Moreover, in the case of avascular cornea this accelerated diffusion would tend to be of greater value than in vascular granulation tissue surrounding lesions elsewhere.

It is of interest to note that Campbell and Ferguson (1950) found that during the healing of heat injuries in subscorbutic guinea-pigs there was a greater tendency to corneal vascularization than in control animals with an adequate intake of ascorbic acid. The stimulus for this neo-vascularization may have been the increased metabolism of the healing tissue. It is possible that the guinea-pigs were unable to satisfy this increased demand from their reduced levels of ascorbic acid.

The original object of this study was to investigate whether the conclusions drawn by Campbell, Ferguson, and Garry (1950) from experiments on guinea-pigs could be applied to human beings. Therefore the study was restricted to small ulcers of a type which would be expected to heal with the usual treatment within a week or 10 days. It is unnecessary, of course, to give ascorbic acid normally to cases of this type. Our findings, however, greatly strengthen the clinical reports of Lyle and McLean (1941), and of Summers (1946), who reported on the effect of massive doses of ascorbic acid on a variety of serious corneal conditions.

We now feel that our results justify a critical study of a carefully controlled series of some of the graver but less common corneal conditions.

Summary

Fifty-one cases of small acute corneal ulcers were examined, and healing time ascertained by instillation of sodium fluorescein under standard arbitrary conditions.

Approximately half the patients received 1.5 g. of ascorbic acid daily; the remainder were given control tablets.

Deep ulcers healed significantly more slowly than superficial ulcers.

The administration of large doses of ascorbic acid had no significant effect upon the healing time of superficial ulcers, but significantly accelerated the healing of deep ulcers.

It is suggested that there may be a localized area around the site of regenerating corneal collagen where the ascorbic acid level falls below the optimum for rapid healing. Raising the general ascorbic acid level with massive doses increases the local rate of replacement.

Pyorrhoea occurred significantly more frequently in patients with corneal ulcers than in others with non-infective eye complaints.

We wish to thank Drs. J. Pendleton White, J. Hill, A. Wright Thomson, and A. Mellick, of the Glasgow Eye Infirmary, for permission to examine their patients. We also wish to express our gratitude to Professor R. C. Garry and Dr. J. B. deV. Weir for their kindly criticism and encouragement. We are indebted to Roche Products Ltd. for a liberal supply of control tablets and of tablets of ascorbic acid, and to the Rankin Medical Research Fund of the University of Glasgow for defraying the cost of this investigation.

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Courses of instruction on medical aspects of atomic warfare at the Royal Naval Medical School, originally started for medical officers of the Royal Navy, have been made available to wardmaster officers in the Royal Navy, to medical officers of the R.N.V.R., and to certain civilian members of the nursing profession. These courses were started in 1948. At first they were intended only for Naval medical officers, but soon it was decided that medical officers of the R.A.M.C. and R.A.F. should attend. In January, 1949, the doors were thrown open to civilian medical officers nominated by the Ministry of Health. The medical officers' standard course lasts five and a half days, and the subjects dealt with include atomic physics, effects of radiation in the human body, monitoring and defence organization, and treatment of casualties. The lectures are supplemented by films. Early this year shorter courses lasting three days for nursing officers of the three fighting Services were started, and these were also opened to members of the civilian nursing profession nominated by the Ministry of Health. In August the Admiralty decided that it was desirable that medical officers of the R.N.V.R. should be given an opportunity of attending similar courses of instruction, and these started in September. About the same time it was decided that dental officers of the R.N. and R.N.V.R., who, especially in wartime, play an important part in all medical defence organizations, should attend these short courses. There is a permanent staff of lecturers at the Royal Naval Medical School, and in addition lectures are given on special subjects by outside lecturers.

INTRAPERITONEAL INTESTINAL ANASTOMOSIS IN COLECTOMY

BY

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Below is presented a short series of 15 cases of strictures and ulcers of the colon (mostly carcinomas) treated by excision with intraperitoneal end-to-end anastomosis, both with and without colostomy.

A good deal has been written about these methods in the American literature from 1942 onwards, representative papers being those of Stone and McLanahan (1942), Wangensteen (1945), Waugh and Custer (1945), and Lahey (1946). In the British literature, however, there is a singular dearth of information on this subject in the last eight years—that is, since the new chemotherapeutic agents have altered the principles of colon surgery.

It is probable, therefore, that the extraperitoneal methods of Paul and Mikulicz are still in vogue up and down the country in cases that would be eminently suitable for an intraperitoneal method. I would at once agree that the latter method requires a certain standard of surgical skill in making an anastomosis, especially in accurate mucosal apposition, but where this exists I suggest that the end-to-end anastomosis is a much better procedure mechanically Risk does not seem to be great in reasonably selected cases It can, of course, be a good deal more radical than an extraperitoneal excision.

In contrast it might be said that a good deal of trouble can be associated with the extraperitoneal methods, not always reflected in textbooks and writings on the subject. Every practical surgeon will know how difficult it can be to get satisfactory crushing of a spur because of the interposition of painful mesenteric structures or the repeated slipping of the enterotome. An extraperitoneal closure in the presence of a partially crushed spur is always difficult and unsatisfactory, and may leave some degree of stricture. At all events, a colon firmly fixed to the abdominal wall can hardly function as well as a mobile colon in its correct anatomical position and with a properly constructed end-to-end anastomosis. So long as the risks of the two procedures were so different these facts were of no account; but now I believe that the difference in risk is slight in selected cases, and these facts should be given full weight in any decision on the correct line of treatment in a particular case.

The period in hospital for a primary colectomy need be no longer than for any other "clean stitch" case—approximately 14 days. If a colostomy has been done this will add another two weeks; the stay should therefore seldom exceed a month. Many a patient subjected to an extraperitoneal method will have been in hospital a good deal longer than this, and probably has had to undergo multiple attempts at spur-crushing and colostomy closure This inevitably leads to a serious loss in his earnings as the weeks go by.

Selection of Suitable Cases

I wish to exclude rectosigmoid lesions from this discussion, as I have had no experience in these primary anastomoses, but there seems to be no good reason why any lesion of the colon should not be resectable by this method at one operation or be made resectable after the establishment of a simple colostomy to overcome the acute

Presentation of Cases in Tabular Form

Case	Date First Seen	Sex	Age	Type and Site of Lesion	Brief Clinical Findings	Operative Treatment	Type	Abdominal Complications	Histology	Result August, 1950
1	Aug. 1946	M	37	Carcinoma of descending colon. Acute colonic obstruction	Three weeks' gradual increase in abdominal pain terminating in colonic obstruction	Transverse colostomy for obstruction: 20 days later resection of descending colon, with aseptic end-to-end anastomosis	Operable	Faecal fistula L.I.F. Now has Devine defunctioning transverse colostomy and reconstructed left colon	Adenocarcinoma of colon. No involvement of mesenteric nodes	Alive and well. No evidence of recurrence
2	Apr. 1947	M	49	Carcinoma of transverse colon. Adherent small gut with small gut obstruction	24-hour emergency with obvious small-gut obstruction and a mass in the right epigastrium	Resection transverse colon and loop of small gut, with double end-to-end open anastomoses. Added caecostomy	Operable	*Nil.* First-intention healing: caecostomy healed spontaneously	Columnar-celled carcinoma with simple adenitis of both mesenteries	Alive and well 2 years later. Now untraced
3	Mar. 1948	F	38	Carcinoma of sigmoid colon. Acute colonic obstruction	Colonic obstruction 7 days. Gross distension	Laparotomy—caecostomy: 6 weeks later resection of sigmoid colon with open end-to-end anastomosis	Operable	Organic small-gut obstruction fifth day from adherence to anastomosis. Operative relief	Tubular columnar-celled carcinoma of sigmoid colon. No involvement of lymph nodes	Died Oct., 1949. Carcinoma of ovaries, probably 2nd primary
4	Nov. 1948	F	71	Carcinoma of descending colon. Chronic colonic obstruction	Abdominal colic and increase in constipation—6 to 8 weeks. Barium enema diagnosis	Resection of left colon with open end-to-end anastomosis between left transverse and mid-sigmoid. Added caecostomy	Operable	*Nil.* First-intention healing: 5 weeks later, extraperitoneal closure of caecostomy	Undifferentiated polygonal and spindle-celled carcinoma of colon. Nodes not involved	Alive and well
5	Dec. 1948	F	67	Carcinoma of descending colon. Non-obstructive	Refractory anaemia whilst under treatment for fractured tibia. Mass L.I.F. Barium enema diagnosis	Resection of left colon with open end-to-end anastomosis between left transverse and mid-sigmoid	Inoperable; liver secondaries	*Nil.* First-intention healing	Tubular columnar-celled mucous carcinoma of colon	Died June, '50. Multiple secondaries
6	Feb. 1949	F	73	Carcinoma of caecum. Chronic obstruction	R.I.F. pain 7 weeks, with occasional abdominal colic; bloody diarrhoea 7 weeks. Loss of weight 1 stone (6·35 kg.)	Right hemicolectomy, with open end-to-end ileo-transverse anastomosis	Operable	*Nil.* First-intention healing	Ulcerated tubular polygonal-celled carcinoma of colon. Nodes negative	Died of cerebral haemorrhage, early 1950
7	May 1949	F	61	Carcinoma of caecum. Chronic obstruction	Pain right lower abdomen 5 months; 1 month colic with borborygmi; vomiting 2 weeks; diarrhoea 1 month. Mass R.I.F.	Right hemicolectomy, with open end-to-end ileo-transverse anastomosis	Inoperable because of involved nodes to root of mesentery	*Nil.* First-intention healing	Columnar-celled carcinoma of colon with involvement of lymph nodes	Died July, '50, jaundice. Lymph spread to liver
8	June 1949	M	78	Carcinoma of transverse colon. Acute and chronic colonic obstruction	Central abdominal colic 8 weeks; vomiting at intervals 6 weeks; increasing constipation 3 months, relieved diarrhoea. Barium enema diagnosis	Caecostomy; 16 days later resection of transverse colon, with open end-to-end anastomosis	Operable	*Nil.* First-intention healing; extraperitoneal closure; caecostomy 15th day	Tubulo-papillary columnar-celled carcinoma of transverse colon. No node involvement	Alive and well
9	July 1949	F	68	Diverticular stricture, lower end sigmoid	Occasional abdominal colic 3 to 4 days 2 or 3 times a year for 8 to 9 years; constipation for 6 weeks. Barium enema: stricture sigmoid. Carcinoma could not be excluded	Resection of sigmoid, with open end-to-end anastomosis between mid-descending colon and lower sigmoid	—	Stricture at anastomosis, with diarrhoea for 20 to 24 days. First-intention healing	Diverticulitis	Alive and well
10	June 1949	F	44	Carcinoma of mid-sigmoid. Colonic obstruction	Onset 3 months previously with abdominal colic and diarrhoea; since then aching lower abdominal pain; occasional colic P.R.—hard mass high in pelvis	Resection of sigmoid with open end-to-end anastomosis	Inoperable; widespread peritoneal metastases	*Nil.* First-intention healing	Tubular columnar-celled carcinoma of colon	Died Nov., '49. Carcinoma cachexia
11	Oct. 1949	F	68	Carcinoma of transverse colon. Colonic obstruction	Colic and increasing constipation 6 months; absolute constipation 2 days; angina of effort 2½ years; colonic distension. Barium enema diagnosis after caecostomy	"Blind" caecostomy; 8 days later, resection of transverse colon, with open end-to-end anastomosis	Inoperable; liver metastases	*Nil.* First-intention healing; extraperitoneal closure of caecostomy 16th day	Tubular columnar-celled carcinoma of colon	Died May, '50
12	Nov. 1949	F	60	Carcinoma of caecum. ? Acute appendix	13 hours pain R.I.F.; nausea; vomited once; bowels loose since onset; bowel habit normal; guarding and tenderness R.I.F.	Right colectomy with open end-to-end anastomosis between ileum and mid-ascending colon	Operable	*Nil.* First-intention healing	Columnar-celled carcinoma of colon. Inflammation of related nodes	Alive and well
13	May 1949	M	72	Carcinoma of iliac colon. Colonic obstruction	Right hemicolectomy 15 years ago, with gross pararectal incisional hernia; colonic obstruction relieved by ileostomy. Barium enema diagnosis	Resection of iliac colon with open end-to-end anastomosis between descending colon and mid-sigmoid	Operable	*Nil.* First-intention healing; later unilateral exclusion for ileostomy	Tubular and columnar-celled carcinoma of colon. Nodes not involved	Alive and well

Presentation of Cases in Tabular Form (Cont.)

Case	Date First Seen	Sex	Age	Type and Site of Lesion	Brief Clinical Findings	Operative Treatment	Type	Abdominal Complications	Histology	Result August, 1950
14	Oct. 1949	M	45	Carcinoma of caecum presenting as probable appendicular abscess	Tender mass R.I.F.; treated conservatively; partial resolution. Barium meal and enema. Bilateral pulmonary T.B. with upper right thoracoplasty; considered quiescent	Explored for probably appendicectomy; right hemicolectomy for carcinoma of caecum with end-to-end ileo-transverse anastomosis	Operable	Died 2nd day, pulmonary insufficiency. P.M.: abdomen satisfactory; chest active	Tubular columnar-celled carcinoma of colon	Died 2nd day
15	July 1950	F	56	Constricting carcinoma below splenic flexure. Partial colonic obstruction	18 months previously abdominal colic 1 week; 1 month previously recurrence of colic with constipation for 1 week, relieved by aperient. Barium enema diagnosis	Left hemicolectomy with open end-to-end anastomosis between mid-transverse and upper sigmoid colon	Operable	*Nil.* First-intention healing	Alveolar tubular columnar-celled mucinous carcinoma of colon infiltrating to serosa. Lymph nodes negative	Alive and well

obstructive element. It is obvious that a safe anastomosis cannot be made in an acutely dilated thin-walled proximal gut with highly infective contents. In these conditions no sulphonamide therapy is possible, and, even if it were, in my opinion an anastomosis within the peritoneum would not be permissible. On the other hand, the presence of chronic obstruction is not always an absolute bar, as in Case 7. Here, owing to hypertrophy and dilatation of the distal ileum from a stenosing growth at the ileo-caecal valve, an anastomosis between the ileum and transverse colon was technically easier than usual because of the similarity of the lumina. In general it may be said that those lesions disclosed in the early stages by barium enema will be suitable for primary resection after adequate pre-operative preparation, while those presenting with some clinical degree of colonic obstruction will require proximal colostomy, barium enema to locate the lesion, and resection after preparation.

Influence of Site of Lesions

Again, I consider that no particular site precludes a primary resection or an end-to-end anastomosis. In the main the accepted resections have been performed with ileo-transverse anastomosis for right colon lesions, transverse-transverse anastomosis for transverse colon lesions, and transverse-sigmoid anastomosis for left colon lesions.

These procedures are perhaps the best, as the blood supply to both ends is more assured, and one is joining two pieces of bowel entirely covered by peritoneum. The mobilization for the transverse-sigmoid anastomosis has to be extensive; but this is the whole secret of the operation, or, for that matter, of any operation on the colon. However, on both the right and the left colon I have done less than the classical resection (see Cases 3, 10, 12, and 13), and performed a successful anastomosis with both the ascending and descending parts of the colon. It would seem, then, that even the retroperitoneal parts of the colon can confidently be used for this procedure.

Type of Anastomosis

Excluding Case 1, all these patients have had an open end-to-end anastomosis, in some cases with crushing-clamps and in some without any type of clamp whatever; the technical minutiae of my ideal anastomosis, however, are dealt with in detail below. To my mind the important thing is accurate mucosal apposition, and I have therefore avoided the aseptic methods. An end-to-end anastomosis undoubtedly seems the method of choice, as it leaves no blind ends to leak or later "blow out." It restores continuity in anatomical manner with no mesenteric overlap. It is applicable to all parts of the colon, be they completely peritonized or not, and marked difference in the two lumina is no contraindication. This can either be dealt with by partially closing the larger piece of gut or, better still, by cutting the smaller so obliquely that they fit. In Case 12 I anastomosed a contracted ileum to the mid-ascending colon (difference of lumina of about three times) by cutting the ileum extremely obliquely. The lines of section must always leave a shorter antemesenteric border to ensure blood supply (Fig. 1). This device also allows of a larger anastomosis and obviates stricture formation.

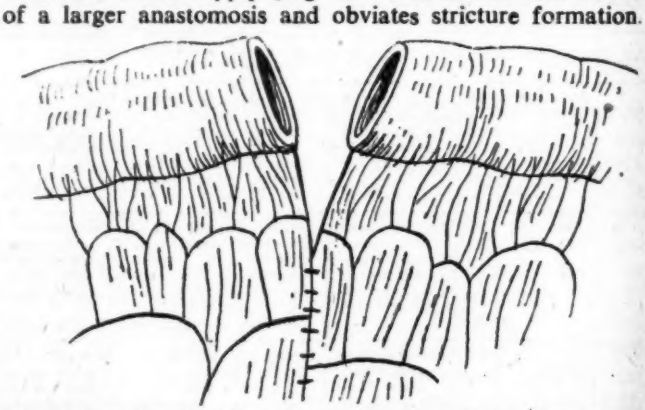

FIG. 1.—Showing the oblique line of section of the bowel to ensure its antemesenteric blood supply.

Effect of Chemotherapy

Undoubtedly the sulphonamide drugs administered in an insoluble form pre-operatively are an important added safety factor in this operation, and have given one a confidence in the intraperitoneal method which the older generation of surgeons can never have had. If, however, one exposes a colonic lesion by exploratory laparotomy the fact that no insoluble sulphonamide preparation has been given is no contraindication to a successful resection by the intraperitoneal method (see Cases 2 and 12). In these cases parenteral sulphonamide was given in the immediately post-operative days, and later the insoluble sulphonamide when feeding was resumed. With streptomycin now generally available I would add this drug in a dosage of 1 g. thrice daily, intramuscularly, and no doubt it will find a place as a further safeguard in the routine care of these cases.

Routine Management

Pre-operative Care

Diet: Low-residue high-calorie diet, with more than adequate amounts of fluid, and glucose to the limit of tolerance. *Sulphonamide Therapy:* Phthalyl sulphathiazole

1 g. thrice daily for five days. *Vitamins:* One "multivite" tablet is given thrice daily. A depot injection of 100 mg. of vitamin K is given intramuscularly, as deficiency in this vitamin can occur, especially with prolonged debacterializing of the gut with sulphonamide therapy. In these circumstances haematoma in the mesentery or suture line may be disastrous and lead to faecal fistula or peritonitis. *Activity:* The patient should be reasonably ambulant during this preparation. Routine breathing and leg exercises are given. *Blood Examination:* This is routine. Any anaemia is corrected by transfusion a few days before operation or, in the presence of a cardiac lesion as in Case 11, by intravenous iron ("ferrivenin," 5 ml. alternate days). *Enemata:* The lower bowels are emptied by a saline enema every second day, one being given the night before operation. *Aperients:* No pre-operative aperient has been given to these cases.

In cases with colostomy the preparation is the same, and sulphonamide by mouth will adequately debacterialize the distal colon by spillage.

Anaesthesia

Premedication: Omnopon 1/3 gr. (22 mg.); scopolamine 1/150 gr. (0.43 mg.), or if over 60 years morphine 1/6 gr. (11 mg.) and atropine 1/100 gr. (0.65 mg.). *Method:* Induction by intravenous thiopentone followed by cyclopropane and oxygen, with intravenous curare added if further relaxation is required.

Operative Procedure

The Approach.—Various incisions have been used during the series. I find a right paramedian rectus-displacing incision best for right hemicolectomy where the anastomosis is near the midline, while for the left colon a left lower oblique muscle-cutting incision is probably better, as the anastomosis is to be in the left iliac fossa region.

Steps of Operation.—(1) General exploration, including local examination of the lesion and lymphatic drainage and examination of the liver and peritoneum. (2) Mobilization of the lesion; and again I wish to stress that the secret of easy colectomy is adequate mobilization, with the lateral aspects of the colon displaced towards the midline. (3) V-shaped mesenteric incision to the root of the mesentery, generously including the lymphatic drainage. (4) Closure of the mesenteric wound up to 1 to 1½ in. (2.5 to 3.75 cm.) of the mesenteric angle (Fig. 2). (5) Application of crushing-clamps on the side of the bowel to be removed, both placed obliquely as in Fig. 1, but one more so than the other to allow the cut lumina to be equalized (Fig. 2). (6) Application of proflavine pads to exclude wound edges, and small pad brought through the defect in the mesentery to protect it. (7) Application of occlusive clamps to the bowel 2–3 in. (5–7.5 cm.) above and below the lines of section. (8) Section of bowel and removal of specimen. (9) A continuous all-coats stitch, starting at the antemesenteric border, is inserted. It runs down the posterior edges and, turning in the mesenteric angles, comes back anterior to finish again at the antemesenteric border (Fig. 3). The stitch is a simple over-and-over one. (10) Mesenteric proflavine pad and the wound pads removed; the hands are thoroughly washed and rinsed in biniodide of mercury; closure of the mesenteric wound is completed; and interrupted seromuscular stitches of medium linen thread or Chinese silk are placed to cover the first layer completely. (11) The anastomosis is now dusted with proflavine–sulphonamide powder, and the wound closed in layers without drainage. If, however, there is the slightest doubt about the security of the union a small soft tube placed down to this area for five days does no harm.

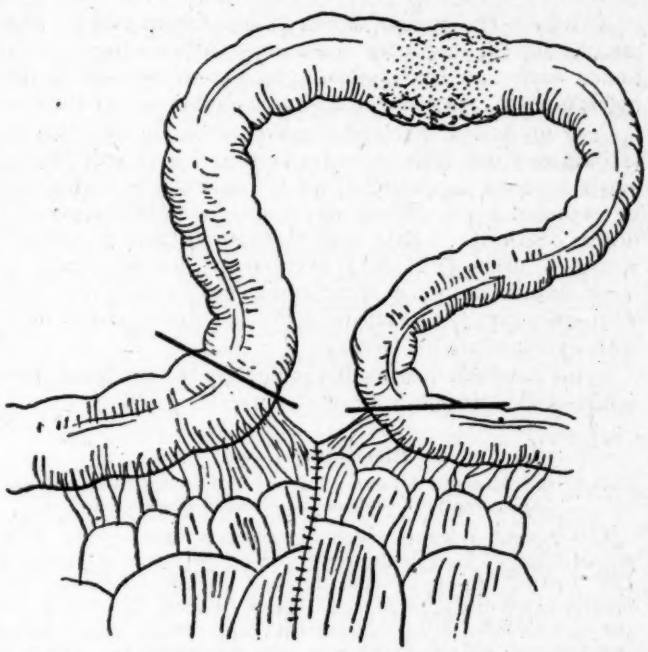

FIG. 2.—Demonstrating the differing obliquity in the lines of section to equalize lumina for suturing. (The mesentery of the loop for excision has been omitted for clarity.)

Post-operative Care

Diet.—It is necessary to avoid anything by mouth until intestinal activity is audible subsequent to the post-operative paresis, usually after 48 hours. During this time fluid balance will require to be maintained by intravenous or subcutaneous saline. Thereafter clear fluids should be given by mouth—1 oz. (28 ml.) for four hours, 2 oz. (57 ml.) for four hours, then stepping up fairly rapidly. Nourishing fluids will be taken 24 hours after this, and phthalyl sulphathiazole therapy resumed; next day a light diet with little roughage will be started, being continued for approximately ten days, until the bowels are well opened. Thereafter the diet can become more varied.

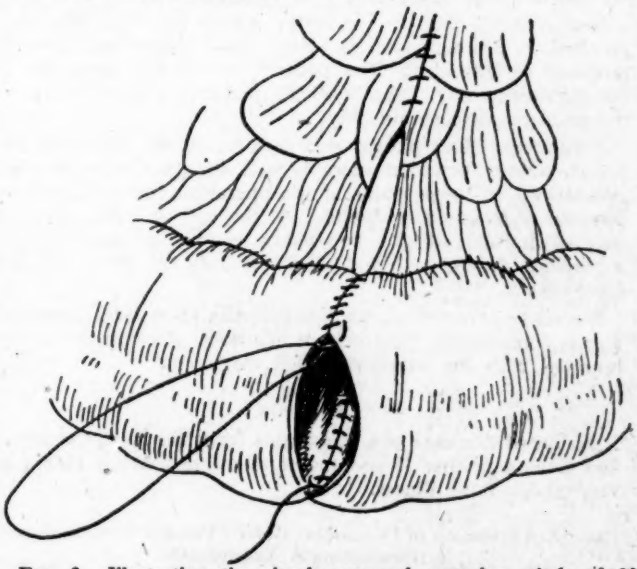

FIG. 3.—Illustrating the simple mucosal apposing stitch of 00 chromic catgut. This is applied first, as the anastomosis can be rotated for the insertion of the interrupted seromuscular stitches behind.

Activity.—The patient should be lifted from bed for five minutes on the day after operation. This routine is continued each day for gradually increasing periods in the bedside chair. Leg and breathing exercises are continued.

Care of Bowels.—A rectal examination on the fifth to seventh day will often reveal a rectum full of soft faeces, and a glycerin suppository will aid evacuation. This can be repeated every second day until spontaneous evacuation is obtained. I have used a simple aperient in syrupus sennae ½ dram (1.75 ml.) twice daily, on the ninth to tenth day to ensure a spontaneous evacuation. In cases with colostomy the problem is not so urgent, but is dealt with in the same manner.

In my submission penicillin is not needed for these cases unless some definite indication presents.

Illustrative Cases

Case 7: Carcinoma of Caecum: Primary End-to-end Intraperitoneal Anastomosis in Presence of Chronic Obstruction

This patient, a woman aged 61, was first seen in May, 1949, complaining of pain in the right side of the lower abdomen of five months' duration. She vomited on one occasion, and latterly had had a good deal of malaise. For the last four weeks she had colicky lower abdominal pain, which was relieved after audible borborygmi. Vomiting was fairly frequent over the latter period. There had been anorexia for two weeks and diarrhoea for a month, with a loss of weight of 10 lb. (4.5 kg.).

Examination showed her to be a spare old lady. Her tongue was dry, the pulse 100, blood pressure 190/100 mm., and haemoglobin 84%. The abdomen was slightly distended, showing visible peristalsis and a tumour in the right iliac fossa.

Operation.—This was carried out through a right mid-paramedian incision under a general anaesthetic. A posterior carcinoma of the ileo-caecal region was found to be penetrating into the retroperitoneal tissues, closely related to the right bladder fundus. There was some free fluid. Involved nodes to the root of the mesentery; the ascending colon and hepatic flexure, and the growth, were mobilized; the bladder was entered and repaired. Right hemicolectomy with end-to-end ileo-transverse junction was done by the open method. In this case the ileum was grossly hypertrophied and dilated, making the anastomosis easy. The wound was closed in layers, with a soft drain to the anastomosis from a stab incision in the loin, and an indwelling catheter was placed in the bladder.

Histology.—The growth was a columnar-celled carcinoma of the caecum with involvement of lymph nodes.

Post-operative Course.—Smooth. Drain removed fifth day; no leak. Bowels opened sixth day. Indwelling catheter removed seventh day. The patient was fit for discharge on the eighteenth day. She received phthalyl sulphathiazole in the post-operative period only.

Follow-up.—This patient was seen at regular intervals, and for 18 months remained tolerably well, though she occasionally complained of vague pains at the operation site for which no physical signs could be found. At the end of June, 1950, she was readmitted with a two-weeks history of jaundice and increasing drowsiness, and died on July 9, 1950, of liver insufficiency.

Necropsy revealed obstructive jaundice from large lymphatic glands compressing the common bile duct. Lymph nodes were involved with the columnar-celled carcinoma.

Comment

Although this case was inoperable from the start, the patient was given a further 18 months of tolerable comfort before her very short fatal illness.

Case 15: Carcinoma of Descending Colon: Primary Open End-to-end Intraperitoneal Anastomosis

A woman aged 56 was first seen in July, 1950, giving the following history. Eighteen months previously she had had colicky lower abdominal pain lasting a few days. Thereafter she was symptomless until one month before admission, when she had a recurrence of the colicky abdominal pain with constipation, which refused to respond to purgatives for one week. After this she began to pass loose stools, and the colicky pain gradually subsided. General, abdominal, and rectal examinations were negative. A barium enema revealed a 2½-in. (6.25 cm.) stricture of the colon just below the splenic flexure.

Operation.—General anaesthesia. Long left paramedian incision. Mobilization of transverse colon, splenic flexure, descending and upper sigmoid colons. A large subsplenic growth was found, with soft nodes in the peripheral group spreading as far as 6 in. (15 cm.) from the growth; no spread to the root of the mesentery. Removal of mobilized colon specified, with mesenteric closure. Primary open end-to-end anastomosis between mid-transverse colon and mid-sigmoid. Wound closed in layers without drainage.

Histology.—Alveolar and tubular columnar-celled mucinous carcinoma of the colon, infiltrating to the serosa. Slight chronic inflammation of lymph nodes.

Post-operative Course.—Smooth. Patient required parenteral fluids for the first two days, and during this time was given 1 oz. (28 ml.) water by mouth hourly. On the third post-operative day bowel sounds were heard; fluids by mouth were slowly increased to 4 oz. (114 ml.) hourly. Phthalyl sulphathiazole recommenced by mouth. On the fourth day nourishing fluids were given. On the sixth day a rectal examination revealed soft faeces in the rectum. A glycerin suppository now produced an evacuation. Light diet was started. Thereafter convalescence was uninterrupted, and the patient was ambulant from the second post-operative day.

Discussion

This small series suggests that the procedure described can be accomplished with a good degree of safety. There were no faecal leaks apart from Case 1, not anastomosed by the recommended method, and it would be fair to say that on the whole convalescence has been really smooth and has given little anxiety. When it is remembered that seven of these patients were over 65 years of age and four of them were over 70, it may well be considered that the powers of colonic healing are greater than we have been led to believe in the past.

Two complications are worthy of mention. In Case 3 a small-gut obstruction occurred from adherence of a loop of small gut to the anastomosis. This required a re-exploration on the fifth day and separation of the small-gut loop. In Case 9 a stricture occurred at the recto-colonic junction owing to the technical error of not cutting the end for anastomosis obliquely enough to give an adequate lumen. The patient suffered from chronic colonic stasis with overflow diarrhoea for some ten days before normal bowel function gradually became restored. This condition was no doubt due to the local oedema at the anastomosis subsiding and natural dilatation occurring through the passage of faeces.

One remaining point I wish to note is the beauty of the operation for cases such as 5, 10, and 11, which were obstructing carcinomas and irremovable metastases. These patients had "clean stitch" operations, and were allowed to leave hospital in a reasonable time to enjoy what life was left to them without the added burden of a colostomy.

Summary

A series of 15 cases of intraperitoneal end-to-end anastomosis after colectomy is presented.

Extra- and intraperitoneal methods are compared.

Factors influencing the choice of operation and the type of anastomosis are discussed.

The detailed management of an intraperitoneal colectomy is given.

Results and complications are discussed.

I wish to thank Sir Henry Souttar for permission to treat these cases and for much helpful advice and criticism, and Dr. Joan Martinez for the skilful anaesthesia which contributed so much towards their recovery.

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The illustrations were redrawn by Miss Sylvia Treadgold from sketches supplied by the author.

EXERCISES IN THE BATH

BY

Sir LEONARD HILL, F.R.S.

The function of the heart is to deliver blood to the capillaries: aided by the valves in the veins and the suction and belly-compressing action of the respiratory pump, and in the active animal by the contraction of skeletal muscles and the frequent changes of posture overcoming the influence of gravity, the blood is returned to the heart by the great veins and without effort on its part. All parts of the body secure an adequate circulation and supply of oxygen, and waste substances are removed. In the sedentary man, inactive, with legs dependent, and gravity acting against the return of blood, the conditions are not so good. Parts of the body may be less well oxygenated and waste products not so well removed by the circulating blood. More work is thrown on the heart by less aid being given to the return of venous blood, and this may possibly contribute to heart disease in the elderly. In recumbency, with the turning movements that take place in sleep, there is a more even circulation, with removal of fatigue. Immersed in water a 10-stone (63.5 kg.) man weighs only 10 lb. (4.5 kg.). The economy of energy needed for muscular movement carried out under water is then immense.

Mr. T. R. Togna has developed a system of exercise and massage in the bath which set him free from minor troubles of health, and has kept him in such good condition that at the age of 77 he can easily run 81 yards (74 metres) in 12 seconds.

The oxygen pulse (that is, the volume of oxygen used per pulse beat) given by several observers for various adults doing exercise in air ranged from 7 to 13 c.cm. of oxygen intake per beat with a pulse frequency ranging from 120 to 174. The marathon runner De Mar, with a pulse of 118, had an oxygen intake per pulse beat of 17 c.cm. This figure is equalled by Mr. Togna, when doing his exercise with autonomous massage in the bath, with a pulse frequency of 66 beats, 6 beats above his basal.

The exercises performed in water are associated with a large absorption of oxygen per pulse beat—a sign of a higher degree of efficiency of circulation throughout the body. Togna tells me that in his youth he followed scientific and literary studies of a general nature and was always especially interested in problems of health. At the age of 52, while in his bath, he noticed that, by performing vigorous contractions which were bringing into play the body skeletal muscles, his pulse rate did not increase according to his experience in air and when swimming. This fact impressed him. He became intrigued with the meaning of it, and started studying textbooks on the physiology of activity. By making a habit of the activity its beneficial effects became obvious to him.

His theory was established in effect by the experiments of Professor G. P. Crowden in September, 1933, which were reported in the proceedings of the Physiological Society (*J. Physiol.*, 1935, **84**, 31P).

TABLE I.—*Results of Observations Carried out on Mr. Togna*

(a) Conditions When Tests were Taken	(b) Volume of Air Breathed (c.cm./min.)	(c) Oxygen Consumption (c.cm./min.)	(d) Carbon Dioxide Production (c.cm./min.)	(e) Pulse Rate (Beats per min.)	(f) Oxygen Consumption per Beat (c.cm.)	(g) No. of Movements (per min.)	(h) Blood Pressure	(i) Respiration Rate (per min.)
Basal (reclining)	12,800	282	192	60	4·7	—	140/58	15
Standing run	37,000	1,848	1,860	124	14·9	72	170/78	24
Bath exercise:								
Type I—arm and leg bending	21,000	890	736	72	12·3	42	132/58	15
Type II—trunk raising	24,500	970	840	68	14·3	46	132/54	15
Type III—head, face, neck, and back massage, with simultaneous expansion and contraction of chest and abdomen and leg bending	27,800	1,135	1,080	66	17·2	30	132/55	15
One hour after (reclining)	12,600	400	342	66	6·0	—	142/54	16
Two hours after (reclining)	10,100	330	274	64	5·2	—	146/56	18

TABLE II.—*Exercise in the Bath Performed by Healthy Subjects for the First Time*

(a)	(b) Volume of Air Breathed (c.cm./min.)	(c) Oxygen Consumption (c.cm./min.)	(d) Carbon Dioxide Production (c.cm./min.)	(e) Pulse Rate (Beats per min.)	(f) Oxygen Consumption per Beat (c.cm.)	(g) No. of Movements per min.	(h) Blood Pressure	(i) Rate of Respirations per min.
Basal Metabolism								
Mr. O. G. (46)	7,470	262	209	78	3·36	—	118/78	13
Miss M. M. (28)	12,500	250	200	72	3·5	—	122/74	16
Miss J. C. (21)	8,400	231	168	76	3·0	—	118/70	15
Exercise in Bath								
Mr. O. G.	18,000	684	630	75	9·1	—	112/66	15
Miss M. M.	14,250	527	399	66	8·0	—	110/66	24
Miss J. C.	9,500	466	366	70	6·66	—	106/56	25
1½ Hours After Resting								
Mr. O. G.	9,500	370	314	82	4·5	—	112/70	12
Miss M. M.	9,750	302	214	70	4·3	—	110/64	16
Miss J. C.	9,000	297	225	72	4·1	—	108/56	18

No pecuniary interest is attached by Togna to his concept, but he has a profound conviction of the benefit of exercises in the bath to his family, his friends, and himself, and a desire to make it known by publication of pamphlets and a book illustrated by photographs. I myself have acquired the habit of these exercises and found them of benefit at my age, now 84, in keeping my body supple and fit in all parts.

There can be no doubt, I think, that these exercises offer a valuable means of bringing at bay the decadence of the ageing processes by keeping up bodily energy, and quite possibly warding off heart disease.

Recently I have had a fresh series of observations carried out on Mr. Togna by the Clinical Research Association to ascertain : (*a*) the oxygen consumption under basal conditions ; (*b*) the increase in oxygen consumption during three types of bath exercises ; (*c*) the rate of oxygen consumption up to two hours after the exercises ; and, for comparison, (*d*) the oxygen consumption while performing mild exercises (standing run) in the air.

The values obtained and the physical conditions are shown in Table I. The results of tests on three subjects exercising for the first time are shown in Table II.

Comment

It will be seen that the criterion by which the value of the exercises must be judged is the oxygen consumption per pulse beat (column *f*) when taken in conjunction with the blood-pressure reading (column *h*). On this basis it will be seen in the case of Togna that with the standing-run exercise in air the oxygen consumption per beat is 14.9 c.cm. : this is accompanied by a marked rise in both the pulse rate and the blood pressure. The exercises in the bath, however, produce a high rate of oxygen consumption per beat (in the case of Type III exercise, more than the standing run in air), and this increased oxygen consumption is obtained with only a slight increase in the pulse rate and accompanied by a drop in the blood pressure. In my case the oxygen consumption per pulse beat increased from 4.0 to 6.2 and the blood pressure fell from 192/96 to 168/86.

The values obtained one and two hours afterwards are interesting ; it will be seen that the oxygen consumption per beat is still increased over the basal value, showing that the increased oxygen consumption is maintained for some time after the tests.

General François Daubenton, of the Netherlands, has been appointed to the post of chief of the W.H.O. Office for Africa. Dr. Daubenton was formerly public health consultant to the W.H.O. Regional Office for the Eastern Mediterranean, and headed the W.H.O. mission in Ethiopia. The newly created W.H.O. office for Africa will be located at Geneva until a permanent regional organization for Africa has been established. Three such organizations have already been set up by W.H.O.—in New Delhi, for South-east Asia ; in Alexandria, for the Eastern Mediterranean ; and in Washington (Pan-American Sanitary Bureau), for the Americas. In addition, a temporary office for the Western Pacific is functioning in Hong Kong, and Geneva is the seat of the W.H.O. Office for Europe. Dr. Daubenton was born in Rotterdam in 1888 and studied in Utrecht, Lausanne, London, and Johannesburg. Before joining the World Health Organization he was Director-General of Medical Services for the Royal Netherlands Army. Before the second world war Dr. Daubenton spent over 20 years in Africa, mainly as chief medical officer to a large Witwatersrand gold-mining group. He was later appointed to various public health posts and acquired a wide knowledge of health problems of the African Continent.

Medical Memoranda

Influenzal Meningitis Treated With Chloramphenicol

Haemophilus influenzae is an important cause of meningitis in Malaya, accounting for 16% of the cases (Green and Mankikar, 1949b). Influenzal meningitis occurs mainly among Indian and Chinese children aged from 2 months to 2 years, the majority being under 1 year. These infections have almost invariably proved fatal, and in our experience the strains of *H. influenzae* isolated have been consistently insensitive to penicillin.

Streptomycin treatment of influenzal meningitis has not been entirely encouraging, and it involves the technical difficulties and infective risks of repeated intrathecal injections as well as the evolution of streptomycin-resistant strains of *H. influenzae*.

Woodward *et al.* (1948) have shown that chloramphenicol given orally reaches a concentration of 20 to 80 μg. in the blood, and according to Smadel *et al.* (1949) it attains about half this level in the cerebrospinal fluid. *In vitro* experiments (Green and Mankikar, 1949a) showed that Malayan strains of *H. influenzae* were readily susceptible to chloramphenicol in concentrations theoretically obtainable in the cerebrospinal fluid when this antibiotic is given by mouth.

With the above findings in view, the use of chloramphenicol was considered to be justified in the following case.

Case Report

A Chinese female infant, aged 4 months and weighing 14 lb. (6.4 kg.), was admitted to hospital in October, 1949, having had continuous fever for the past three weeks and cough and convulsion for the past four days. The head was retracted, the limbs were spastic, and the fontanelle was tense. The cerebrospinal fluid contained pus cells and pleomorphic forms of *H. influenzae* which grew in pure culture. This strain was found sensitive to chloramphenicol and "aureomycin." The sugar in the cerebrospinal fluid was below 15 mg. per 100 ml., indicating, according to Alexander *et al.* (1942), a severe infection.

The contents of one chloramphenicol capsule (250 mg.) were given just before each four-hourly feed, small quantities of the powder being put intermittently into a teaspoon, which was then filled with milk and tipped into the mouth. (The solubility of chloramphenicol is relatively slight—about 2 mg. per ml.) No apparent difficulty was encountered in swallowing or retaining these medicated feeds despite the bitterness of the drug. After five days there was occasional vomiting, with some transient diarrhoea on the tenth day. The amount of chloramphenicol given daily over a period of eleven days varied from 1 to 1.5 g.

The temperature (101° F.—38.3° C.) fell within 24 hours, but rose to 99° F. (37.2° C.) subsequently at intervals during treatment. After two days the spasticity of the limbs lessened, but it remained more pronounced on the left side and there were occasional twitchings of the right hand and the right side of the face. The head retraction was not so marked, and the fontanelle was less tense. There was deviation of the eyes to the left. On the third day no pus cells and no bacteria were seen in the cerebrospinal fluid, which was sterile on culture.

By the eighth day the right leg and arm were being moved freely, but spasticity, though lessened, remained in the left leg and arm. Some distension of the abdomen was present, but this disappeared by the tenth day. By the fourteenth day—three days after chloramphenicol treatment had ceased—there was evidence of general improvement, but there were also

indications of what was regarded as residual inflammatory infiltration of the infected meninges*; that is, the left arm and leg were still somewhat spastic and, when excited, the child's eyes turned strongly to the left. On the sixteenth day the cerebrospinal fluid was found clear and sterile on culture.

After three weeks the left arm and leg were being moved freely, and the deviation of the eyes had ceased. Movements of the left arm and leg became more frequent, and by the twenty-second day movements of the limbs appeared normal with the exception of slight spasticity of the left hand. By the end of the fourth week the spasticity of the left hand had disappeared and recovery was apparently complete.

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Spontaneous Intraperitoneal Haemorrhage due to Haemangioma of Liver

Haemangioma of the liver is common, but few cases give rise to any symptoms. The following case is exceptional in that it caused an acute abdominal emergency.

CASE REPORT

The patient, a man aged 61, was admitted to hospital as an emergency on July 28, 1949. Two and a half days previously he had complained of acute pain in his upper abdomen, which had radiated to his left shoulder. For the past 36 hours he had been vomiting. His bowels had not acted for 24 hours. He gave a long history of "chronic dyspepsia," but investigation elsewhere had on more than one occasion proved negative for peptic ulceration and no definite diagnosis had been made. He had a right inguinal hernia satisfactorily controlled by a truss. There was no history of injury.

On admission his temperature was 101.4° F. (38.55° C.), pulse 124, and respirations 28. His tongue was dry and furred. The heart and lungs showed no appreciable disease. There was acute tenderness with guarding in the epigastrium and right hypochondrium, and this extended into the right flank and down to the right iliac fossa. The left side of the abdomen was relatively free. Bowel sounds were not heard; there was no palpable tumour and no cutaneous angiomata. Examination per rectum revealed some tenderness on the right side only. A provisional diagnosis of perforated duodenal ulcer was made.

Operation.—A right paramedian incision was made, and on opening the peritoneum blood welled out. This was readily seen to be coming from a dark mass at the edge of the left lobe of the liver. The spleen, stomach, duodenum, gall-bladder, and appendix were normal. The sucker was in continuous use withdrawing blood. The diaphragmatic surface of the left lobe of the liver was seen to be covered by a thin-walled angiomatous formation with a clear-cut margin which did not extend to the right lobe. At the anterior edge there was a small perforation through which the blood was escaping. Dr. Stewart Smith, the pathologist, kindly came to the theatre and confirmed the diagnosis of haemangioma of the liver. A wedge biopsy of the growth was taken, including the perforated area, and haemostasis was achieved by mattress sutures over "calgitex" gauze. The wound was closed in layers with drainage.

The patient made a good recovery. He received three pints (1.7 litres) of blood, and, except for a slight discharge from the site of the drainage tube, had an easy convalescence. The report on the histopathology, dated August 5, showed "a capillary haemangioma in the liver with a central large organizing thrombus."

In view of the danger of a recurrent haemorrhage from this growth, a further operation was performed on August 31, with the intention of performing a formal resection of the left lobe of the liver. However, on opening the abdomen through a transverse incision, the left lobe was found to be adherent to the diaphragm and it was thought best to leave well alone. The second incision healed with some delay owing to infection. The patient was discharged on September 22.

COMMENT

When a haemangioma of the liver gives rise to symptoms it usually presents in one of three ways: (1) a mass which is otherwise symptomless is found at laparotomy to have this origin (Morris, 1940, Shumacker, 1942); (2) there are signs of obstruction (Wakeley, 1924–5); or (3) vague dyspeptic symptoms are the complaint, and on laparotomy for some other suspected lesion a haemangioma is found, without any other pathological lesion (Shumacker, 1942).

Very rarely does spontaneous rupture occur, though haemorrhage at operations may be fatal (Mantle, 1903) or exceedingly troublesome (d'Errico, 1946). Ewing (1928) states that it may occur as the tumour slowly increases in size, and that it is usually fatal. When spontaneous rupture does occur the diagnosis of acute appendix, ruptured ectopic, or peritonitis has been made (Marckstradt, 1938). When treatment has been undertaken the tumour has been resected, and the danger of incising the tumour itself has been repeatedly stressed (Mantle, 1903; d'Errico, 1946). Most of the tumours resected have, however, been pedunculated, or it has been possible to form a pedicle.

The above case had the indefinite digestive troubles for which no other cause was found at operation, with the superimposition of the acute surgical emergency. At the first operation resection of the growth would have necessitated removal of the whole left lobe of the liver, a procedure which the patient's condition would not at the time warrant. While cutting the wedge biopsy haemorrhage was controlled by compressing the free edge of the lesser omentum and hepatic pedicle, and on tying the mattress sutures over the haemostatic gauze no further leak occurred. This was probably owing to the capillary nature of the growth as compared with the cavernomata, into which category the reported troublesome tumours fell, and to some extent to the haemostatic qualities of the gauze.

However, at the second operation an attempt to separate the adhesions between the diaphragm and the liver would probably have caused severe haemorrhage, while their presence, on the other hand, greatly reduces the risk of any further spontaneous haemorrhage.

I wish to thank Mr. A. C. Gairdner for permission to publish this case, and Dr. Stewart Smith for the pathological investigation.

K. P. S. CALDWELL, M.A., M.B., F.R.C.S.

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*The following morbid processes were envisaged in relation to the symptoms: the original inflammation of the pia-arachnoid had been followed by the development of purulent exudate in the subarachnoid spaces, especially at the base, and also along the posterior surface of the spinal cord and possibly surrounding the nerve roots.

Reviews

PROBLEMS OF MENTAL DEFICIENCY

The Biology of Mental Defect. By Lionel S. Penrose, M.A., M.D. Preface by Professor J. B. S. Haldane, F.R.S. (Pp. 285; illustrated. £1 1s.) London: Sidgwick and Jackson.

This is not a textbook of mental deficiency, nor is it a monograph dealing exhaustively with a particular aspect of the subject. It will be useful to those who are reading for a diploma in psychological medicine, but covers only a part of their field. Furthermore, sections of it are more suited to the research worker. Professor Penrose writes with the background of twenty years of experience; he writes about the things that have interested him and about the subjects to which he has himself contributed. The data used for illustration are to a large extent his own. Much of the book is a single closely argued sequence. What has interested him particularly is historical development in thought, problems of definition and classification, and, above all, problems of causation. Genetics bulks large because heredity is important in determining mental deficiency; but other factors are important, too, hence the more comprehensive title.

After a brief but admirable historical chapter Professor Penrose passes on to incidence, definition and measurement, and the principles of classification. The next chapter, on problems of causation, describes the genetic and early environmental background of development into which the aetiology of mental defect must be fitted. It is in the following chapter that the more general reader will begin to run into difficulties, for this deals with methods of analysis in human genetics. The research worker, on the other hand, will feel that it does not say enough. But it is a very difficult task to write such a chapter, and most other writers would probably have fared worse. Professor Penrose then turns to the genetics of intelligence, and then to rare dominant, recessive, and sex-linked defects, with a particularly interesting chapter on defects of obscure origin and environmentally determined disabilities. This includes a very good section on mongolism, to which he has himself made many important contributions. It is perhaps a little surprising, though welcome, to find in this part of the book detailed descriptions of the genetics of conditions not ordinarily associated with mental deficiency, such as Huntington's chorea, von Recklinghausen's disease, Friedreich's ataxia, and retinitis pigmentosa. But these are among the things that have interested Professor Penrose, and the book would be poorer without them. The final chapters deal briefly with mental disorders chiefly in relation to mental deficiency, and with the principles of treatment.

Within the limits laid down by the selection of topics and by the method of approach, which I have tried to indicate in the opening paragraph of this review, the book should make a wide appeal. Perhaps it should be regarded mainly as a book by a research worker for research workers, but many others, even if they do not discover in it all they want to know, will find it up to date, well presented, clear in its conclusions, and, above all, stimulating. Not all workers will agree with everything the author says, but the papers of the next few years will be the better for the reasoned arguments that others will be forced to produce if they are to join issue with him.

The only criticism of substance that one feels inclined to make is that when Professor Penrose touches on subjects that do not interest him, or which he regards as not particularly important, he seems to show some impatience, even carelessness. For example, on page 23 he makes it clear that he does not regard it as of much importance that the numbers of persons of various levels of test intelligence, down to very low limits, are just those expected if the distribution of intelligence conforms to the normal curve On pages 24–5 he writes:

"The distribution of Binet scores, expressed in terms of intelligence quotients, is usually found to be fairly symmetrical. This was demonstrated by Terman (1916) and has been confirmed more recently by Roberts, Norman, and Griffiths (1935). A sample of 192 subjects from a survey made in an urban centre, embracing the complete child population of certain age groups, was analysed. Roberts considered that the distribution of I.Q. was Gaussian, with mean value 100 and standard deviation 15 points. The Gaussian form of the distribution was thought to extend as far as about three times the standard error on either side of the mean."

The reader may well be astonished that anyone should talk about what is happening three standard deviations from the mean on the basis of a sample of 192. Should he then turn to the paper quoted he will find no reference to the subject. In the paper, not included in the bibliography, which did deal with this point, nothing was said about a mean of 100 or a standard deviation of 15. It was shown that for a particular population the mean, based on the equivalent of 710 observations, was 98.785; the standard deviation—on the equivalent of 495—was 15.201; and the negative tail of the curve based on 3,361 observations was normal down to about I.Q. 45, or three and a half times the standard deviation (not three times the standard error). There were no data, as is suggested, on the positive side of the curve. I hasten to add that this is the only point in the book where I feel some slight sense of personal grievance. Again, while the genetics of various special conditions are admirably described, some of the clinical descriptions are curt almost to the point of inaccuracy. Thus, oculogyric crises (p. 217) are defined as "transitory inability to move the eyes or eyelids." But such defects, which could easily be corrected in a new edition, are a minor matter in an original and valuable book which represents a notable contribution to the subject.

J. A. FRASER ROBERTS

LIPID METABOLISM

Lipidoses: Diseases of the Cellular Lipid Metabolism. By S. J. Thannhauser, M.D., Ph.D. (Pp. 605; 125 figures. 96s.) London: Geoffrey Cumberlege. 1950.

The first edition of this classic work was published in 1940 The author has found it necessary to make some important alterations, notably in regard to xanthomatous biliary cirrhosis. Thannhauser and Magendantz (1938) thought that this clinical syndrome might be due to xanthomatous scar tissue resulting from xanthoma of the larger bile ducts. Thannhauser has altered his opinion because early biopsies and necropsies have not revealed xanthomatous changes of the lining of the bile ducts. He thinks that the assumption is justified that there is a special type of cirrhosis which MacMahon and Thannhauser designate anatomically as "pericholangiolitic biliary cirrhosis." The section on the Hurler-Pfaundler syndrome (gargoylism) is new, as is also that on infantile amaurotic family idiocy. A very important section is that on eosinophilic xanthomatous granuloma, which is synonymous with Schüller–Christian's syndrome. Not the least interesting addition is the account of the adult

form of Niemann–Pick's disease, the existence of which is now definitely proved—thanks largely to the important study of Rutishauser, Dusendschow, and Pfändler on the cases of two brothers, of which Thannhauser has made good use. Thannhauser writes :

"The adult and infantile forms of Niemann–Pick's disease are as clinically different from each other as are the adult and infantile forms of Gaucher's disease. Both infantile Gaucher's and infantile Niemann–Pick's disease terminate in early death after a rapid and disastrous clinical course involving the entire organism. The adult form in contrast is not manifested by any spectacular complaints. Usually the patients are unaware of their disease until a physician examining them for an intercurrent disease finds an enlarged spleen."

It is specially noteworthy that in the adult form of Niemann–Pick's disease an erythraemic condition and splenomegaly may suggest the diagnosis of the Vaquez–Osler type of polycythaemia or of Ayerza's disease. In Thannhauser's opinion the heart failure and the erythraemic condition in one of the brothers was the result of pulmonary fibrosis, which was revealed by *x*-ray examination and was due (as shown by necropsy) to an intensive involvement of the lung with Niemann–Pick's cells (resulting in fibrosis).

The sections on idiopathic hyperlipaemia and many others have been greatly enlarged.

This review gives no adequate idea of the value of Thannhauser's work, but it may serve to emphasize the interest and importance of the alterations and additions that have been made in the second edition.

F. PARKES WEBER.

BIOLOGY FOR ENJOYMENT

The Human Species: A Biology of Man. By Anthony Barnett. (Pp. 280; 72 illustrations. 18s.) London: MacGibbon and Kee. 1950.

This book, according to the jacket, is addressed "to the general reader and to those beginning the study of biology, for their information and enjoyment." For this public Mr. Barnett has written a book which covers in a small space a great variety of subjects. He ranges from genetics, through embryology, anthropology, and evolution, to agriculture, nutrition, public health, and the study of population problems. The text is clear and concise, and he gives an interesting and stimulating account of many of the main facts, though the first few chapters may contain slightly tougher material than would be conducive to the general reader's "enjoyment." There is a good index, and a bibliography of suggested further reading. The illustrations, on the other hand, are often unsatisfactory. Some of the diagrams are over-simplified to the point of being obscure or misleading, while others are either too complicated or insufficiently explained in the legends. There are two lurid and inaccurate figures of the male and female genital apparatus; surely more suitable diagrams of these could have been found. In spite of a number of corrigenda, cross-reference between illustrations and text is occasionally faulty.

In a book as short as this it is inevitable that there must be a certain bias in the selection and interpretation of facts; in this case the bias is towards the political left. This does not make the book any less entertaining, but it does lead to the occasional appearance of statements such as the unqualified assertion that the Russian atomic explosion in 1949 was part of a vast irrigation project. The evidence available to the general public on this point is hardly as clear-cut as this statement would imply.

D. C. SINCLAIR.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Practical Food Inspection. By C. R. A. Martin. Vol. 1: Meat Inspection. (Pp. 322. 18s.) Vol. 2: Fish, Poultry, and Other Foods. (Pp. 308. 18s.) 4th eds. London: H. K. Lewis. 1950.

Peptic Ulcer. By A. C. Ivy, Ph.D., M.D., D.Sc., LL.D., and others. (Pp. 1,144. 96s.) London: J. and A. Churchill. 1950.

Toxaemias of Pregnancy. Edited by J. Hammond, M.A., D.Sc., F.R.S., and others. A Ciba Foundation Symposium. (Pp. 280. 21s.) London: J. and A. Churchill. 1950.

Carotenoids. By P. Karrer and E. Jucker. (Pp. 384. 65s.) London: Cleaver-Hume Press. 1950.

The Effects of Atomic Weapons. Prepared for and in co-operation with the U.S. Department of Defense and the U.S. Atomic Energy Commission, under the direction of the Los Alamos Scientific Laboratory. (Pp. 456. 25s. 6d.) London: McGraw-Hill Book Company. 1950.

Significance of the Body Fluids in Clinical Medicine. By L. H. Newburgh, M.D. (Pp. 76. 15s.) Oxford: Blackwell Scientific Publications. 1950.

Postgraduate Lectures on Orthopedic Diagnosis and Indications. By A. Steindler, M.D., F.A.C.S. Vol. 1. (Pp. 289. 55s.) Oxford: Blackwell Scientific Publications. 1950.

Bone and Joint Diseases. By J. Vernon Luck, M.S., M.D., F.A.C.S., F.I.C.S. (Pp. 614. 120s.) Oxford: Blackwell Scientific Publications. 1950.

The Human Mind. By Professor S. P. Adinarayan, M.A. (Pp. 195. 7s. 6d.) London: Hutchinson's University Library. 1950.

The Individual's Relation to Reality in Our Culture. By E. F. Hellersberg, Ph.D. (Pp. 128. 25s.) Oxford: Blackwell Scientific Publications. 1950.

Psychological Factors of Peace and War. Edited by T. H. Pear. (Pp. 262. 16s.) London: Hutchinson. 1950.

Carbon Dioxide Therapy. By L. J. Meduna, M.D. (Pp. 236. 36s.) Oxford: Blackwell Scientific Publications. 1950.

Enzymes, Growth and Cancer. By Van R. Potter, Ph.D. (Pp. 64. 12s.) Oxford: Blackwell Scientific Publications. 1950.

On the Experimental Morphology of the Adrenal Cortex. By H. Selye, M.D., Ph.D., D.Sc., F.R.S.C., and H. Stone, B.Sc. (Pp. 105. 16s. 6d.) Oxford: Blackwell Scientific Publications. 1950.

The Trial of Peter Griffiths: The Blackburn Baby Murder. Edited by G. Godwin. Notable British Trials Series, No. 73. (Pp. 219. 15s.) London: William Hodge. 1950.

Les Formes de Début des Cholécystites Chroniques non Lithiasiques. By G. Albot and others. (Pp. 55. No price.) Paris: Vigot. 1950.

Bad Gleichenberg, seine Heilquellen und Kuren. By A. G. Brusselle and others. (Pp. 134. 13s.) Vienna: Springer. 1950.

Die Hemmkörperhämophilie. By E. Deutsch, M.D. (Pp. 112. 27s. 6d.) Vienna: Springer. 1950.

Zur Geschichte der Direkten Untersuchungsmethoden der Oberen Luft- und Speisewege. By C. V. Eicken. (Pp. 14. No price.) Berlin: Akademie-Verlag. 1950.

Das Autogene Training. By Professor J. H. Schultz. 6th ed. (Pp. 325. M. 27.) Stuttgart: Georg Thieme. 1950.

Untersuchungstechnik des Chirurgen. By Professor P. Rostock. (Pp. 330. M. 24.) Stuttgart: Georg Thieme. 1950.

Hygiene und Körperschulung der Frau. By Professor F. A. Wahl. (Pp. 166. M. 16.80.) Stuttgart: Georg Thieme. 1950.

Kallikrein Padutin. By Dr. E. K. Frey and others. (Pp. 209. M. 20.) Stuttgart: Ferdinand Enke. 1950.

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DISPLACED REGISTRARS

One of the difficulties of a State-sponsored medical service is that the political party in power will always be tempted to promise more than it can perform. Mr. Bevan and those speaking for him foresaw a big expansion in the consultant and specialist services of this country, and in one of the early debates on the Health Service it was suggested that the number of consultants and specialists would have to be increased by 50%. Even as late as four weeks ago, Lord Haden-Guest stated in the House of Lords that there were not enough doctors to do the work that was necessary, and in the same debate Lord Moran observed that the consultants now numbered only 56% of the number thought by the Minister to be necessary. The Ministry of Health circular on registrars printed in this week's *Supplement* will therefore come as a shock and a severe disappointment to the many young men and women rash enough to take the Government at its word. The Ministry estimates that there are now approximately 2,800 senior registrars and registrars and that the number for whom training posts can be found is only 1,700. The Ministry suggests, in effect, that 1,100 registrars shall be put into the discard. This is a harsh decision and one which reflects discredit on all those who have allowed this state of affairs to come about.

To gull the public and beguile the medical profession, the Government between 1945 and 1948 held out promises which it must have known could not be fulfilled. The path of the would-be consultant was made attractively easy when compared with the old way and the hard way trodden by his predecessors. Financial disabilities were largely removed by the proposals made in the Spens report, and ahead lay an extended hospital and consulting service in which every patient from John o' Groats to Land's End could receive at any moment the expert medical and surgical assistance the Government promised him. On top of this there were many discouraging features in the proposals for the general-practitioner service, and the young man who thought he could make the grade looked upon the career of a specialist as at least one way of avoiding the rough-and-tumble of a general practitioner's life. The war, of course, resulted in the accumulation of medical men and women who wanted to be consultants. This factor alone increased the number of those who sooner or later had to receive a set-back to their expectations. The medical profession itself was partly to blame in that it did not caution the would-be consultant against hoping for too much, and it could have done this by making much more stringent the conditions for taking higher qualifications.

The National Health Service has now been in existence for nearly 2½ years, but the Ministry has still not made public what are to be the establishments of the hospitals in this country, another factor which makes it difficult to assess accurately the Ministry's estimate of the number of registrars required. But if we accept the figure of between 5,000 and 6,000 as representing the number of consultants and specialists in the country, and the Government's own rough estimate of 50% as being the amount by which the number of consultants should be increased, the present total of 2,800 registrars would seem to be feasible. What must obviously limit the number of registrars at the moment is the number of posts available for them. This number cannot be increased unless there is an extension of existing hospitals and the building of new ones—and, what is as important, enough men and women of suitable competency to man them. This is surely so obvious that the Ministry of Health cannot fail to have been aware of it, and therefore aware of the grave injustice being done to those who have been allowed to train as registrars and are now told—1,100 of them—that they are not wanted. Or at least not in the National Health Service, because in a brief little note at the end of the Ministry circular, under the heading "Other Openings," is information to the effect that there are about 700 vacancies in His Majesty's Forces and in the Colonial Medical Service—in the former of which terms and conditions of service are inferior to those in the N.H.S. It should be pointed out that the Joint Committee has, in its discussions with the Ministry, stressed the need for more consultants. On this point everyone is agreed. Yet the Ministry, apparently on instructions from the Treasury, refuses to do this, refuses in other words to fulfil the promises made by the Government to the people of this country.

The most curious paragraph and one which deserves the closest scrutiny by both registrars and by general practitioners is No. 11 (b). Here is laid down what the Ministry describes as "a long-term method of meeting staffing difficulties in the senior registrar field." This paragraph in the circular begins by noting that "a reduction in the numbers of persons in training in hospitals may necessitate the appointment of other practitioners as assistants in their place." To fill such vacancies, the Ministry's "long-term method" is to appoint general practitioners to work on a part-time basis as clinical assistants and to receive remuneration for this. Such practitioners will normally be expected to have high qualifications and experience as registrars. It will be some time before the full implications of this

proposal become manifest. It might of course be argued that this is one way in which the Ministry could increase the reward of the experienced general practitioner, and one way, too, in which general practitioners could expect to enter the ranks of consultants. It is certainly desirable that facilities for such movement from general practice to consultant work should exist. But can this view of things be expected to appeal to the 1,100 registrars who have been encouraged to believe that they will have the chance of becoming consultants and specialists, provided of course that they satisfy those who are training them that they are so capable? And will this proposal really satisfy those who rightly insist that the general practitioner must find his proper place in the hospital life of this country? The Ministry has no doubt been instructed by the Treasury to discover every possible device for cutting down the cost of the Health Service, and the present proposal looks like a most disingenuous method of securing the registrar-type of service at cut rates, the dispossessed registrars themselves being politely invited to work in the armed Forces under conditions which the Government refuses to make attractive.

If during the 2½ years of its existence the National Health Service has not broken down, it is principally because the medical profession has gone on doing its job in spite of all the irritations and frustrations that come from the fact that such a gigantic scheme, introduced at once instead of by stages, could not possibly be operated efficiently. This is not being wise after the event, because this view was stated plainly enough in these columns and elsewhere before the Service began. The medical profession is prepared to go on doing its job, but if it is to be treated in this summary fashion, and if the Ministry breaks faith with the profession, then it will have to insist upon a different kind of service in which it can work in harmony.

THE "DRYING" OF TUMOURS

Much interest was aroused when in March, 1949, Professor W. E. Gye[1] described some experiments on the transmission of mouse tumours by means of tissues simply frozen at −76° C. or dried from the frozen state. He concluded in this paper, and in subsequent publications along with colleagues, that tumour cells could not survive freezing and drying, and that "a continuing cause" of cancer had been disclosed, "probably viral in nature." Few people were convinced that mere freezing would necessarily kill the cells, for, after all, trypanosomes were known to survive at −76° C., and there was in the literature much other evidence of a similar kind. Many pathologists, however, felt it unlikely that mammalian cells could survive thorough drying. In discussing the work, we asked, "Is it reasonably certain that frozen, pickled, and above all dried tumour tissue does not contain any living mammalian cells at all?"[2] In the last eighteen months this question must have been frequently in the minds of those most interested; and more and more doubts grew about whether drying need kill mammalian cells. In June, 1949, Dr. J. Craigie, who soon afterwards succeeded Professor Gye as Director of the Imperial Cancer Research Fund's laboratories, gave an interesting demonstration at a meeting of the Royal Society of Medicine at Mill Hill. His histological preparations showed how dried tumour tissue lost all its visible structure, but how the normal architecture seemed completely restored on rehydration, the appearance being very little different from that of undried tissue. Craigie in a lecture in November, 1949,[3] made it plain that he was not then prepared to accept his predecessor's sweeping conclusions about the significance of the drying experiments "in the absence of adequate quantitative knowledge concerning . . . ability of the cells to survive under various conditions." In particular, information was lacking about the degree of dryness when the cells were dried, as had been done, in the presence of 5% dextrose. Polge, Smith, and Parkes[4] were able to show that spermatozoa would survive freezing and "drying" in the presence of glycerol.

In the opening pages of this issue we publish three papers by Professor R. D. Passey and his colleagues in Leeds. In the first of these the authors again show that "dried" tumour, seeming to be quite structureless, has its architecture restored by rehydration. They freely admit, however, that "the microscope cannot with certainty reveal if tumour cells are alive or dead." In the second paper the Leeds workers describe how tumour cells grow out in tissue culture after being dried for up to 75 minutes. (They write, however, "It is realized that dehydration is not complete.") Finally, Dr. L. Dmochowski and Mr. A. Millard show by histological study that frozen and dried sarcoma cells embedded in clots and grafted into mice grow out and multiply. These results add to the growing conviction that the methods of freeze-drying hitherto used need not kill all mammalian cells. Neither the papers by Gye and his colleagues nor those in this issue by Professor Passey and his co-workers give full information on the completeness of desiccation attained. The reader remains unconvinced that every particle of tumour, every cell, was quite dry; especially so since none of the workers have done what bacteriologists are doing all the time—drying material and testing it after keeping it in the dried state for days or months. It may be imagined that in this type of work almost any result might be obtainable, according to the

[1] *British Medical Journal*, 1949, 1, 511.
[2] Ibid., 1949, 1, 531.
[3] Ibid., 1949, 2, 1485.
[4] *Nature, Lond.*, 1949, 164, 666.

completeness of the desiccation. Despite these criticisms, most will agree with the authors' final conclusion "that surviving cells and not a virus were responsible for the results attained by Gye and his colleagues."

ANTIBIOTIC SYNERGISM AND ANTAGONISM

It has long been recognized that two, or even more, chemotherapeutic agents acting together may produce effects of which any one of them is incapable in the same dose. For example, there are good grounds for combining penicillin and sulphonamides in treating certain conditions. An extreme instance—no longer of practical interest since the advent of chloramphenicol—is typhoid fever, which according to McSweeney[1] responds to large doses of sulphathiazole and penicillin, although either drug alone is useless. Apart from securing or enhancing therapeutic effect combinations of drugs have been used with the object of suppressing the development of bacterial resistance. In *in vitro* studies Klein and Kimmelman[2] used three, and Carpenter and his colleagues[3] no fewer than four, antibacterial agents together to secure this effect. Its best-known practical example is the use of *p*-aminosalicylic acid with streptomycin.

Much less attention has been given to the possibility that one such drug, so far from aiding another, may interfere with its action. Some interesting examples of such antagonism *in vitro* have recently been observed by Bigger,[4] whose earlier work on sulphonamide–penicillin synergism is well known. In his own opinion these are unlikely to have their counterpart in the therapeutic field, either because these particular combinations of drugs—e.g., sulphathiazole and boric acid—are unlikely to be used or because the concentrations in which antagonism is demonstrable are not reached in the body. A much more serious warning against mutual interference by chemotherapeutic agents is afforded by the recent work of Jawetz, of San Francisco. He and his colleagues[5 6] first showed that the limited and often not complete bactericidal action which is exerted by penicillin on enterococci (*Str. faecalis*) is accelerated by the addition of streptomycin in a concentration which, acting alone, has little effect, but actually diminished by adding chloramphenicol. The acceleration caused by streptomycin, culminating in complete sterilization, of which penicillin alone is incapable, is paralleled in the clinical field by the combined action of the two drugs in enterococcal endocarditis: they will cure this infection when penicillin even in very large doses has failed to do so. The opposite effect of chloramphenicol has also been shown by Jawetz and Speck[7] to operate *in vivo*, at least in the experimental animal. In mice inoculated with *Str. pyogenes* and treated with a single dose given one hour later of either 30 μg. of penicillin or 800 μg. of chloramphenicol the mortality was 20%. When both drugs were given it was 60%. Several variations of this experiment consistently gave the same kind of result: for example, when the dose of penicillin was kept constant and that of chloramphenicol varied, the larger the latter—up to 800 μg.—the higher was the mortality. When the variation was reversed, the larger the dose of penicillin with a constant dose of chloramphenicol the lower was the mortality; but it remained higher than that with penicillin alone. These authors conclude with a warning that "shotgun" antibiotic therapy may sometimes defeat its object.

A possible explanation of this effect is one which has been suggested before by several authors in other but similar connexions. Penicillin is rapidly bactericidal only to multiplying bacteria. If another agent is introduced which inhibits multiplication its bactericidal action may well be prevented. This in fact applies to sulphonamide–penicillin combinations, at least over a certain period of time. Why the ultimate effect here is nevertheless synergic is a complex question, the answer to which is probably to be found in the observations of Klein and Kalter.[8] On this hypothesis it should be a general principle, to which there may be exceptions, not to combine a bacteriostatic with a bactericidal agent of the penicillin type. Of the four chief antibiotics now in use, penicillin and streptomycin are bactericidal, and aureomycin and chloramphenicol are bacteriostatic (or, more correctly, bacteriofrenic, if we are to adopt Bigger's new word for growth restraint). Will it prove that either of the two latter interferes with the action of either of the former? This is a possibility to be borne constantly in mind in any therapeutic attempts with combinations of these drugs.

SURGICAL TREATMENT OF PARKINSON'S DISEASE

The severe disability accompanying advanced bilateral Parkinson's disease causes much suffering in patients and excites the compassion of their relatives and friends. The suggestion that this disability may be relieved by surgery not unnaturally raises the hope of cure, especially in the lay mind. It must be emphasized at the outset that there is no surgical treatment of paralysis agitans. But when rigidity, restriction of movement, and psychological changes are relatively mild and tremor is severe, the latter can be relieved by various forms of surgical attack. Such relief can be gained only at the cost of a loss of power in the affected limbs—varying in severity from a hemiplegia to

[1] *Lancet*, 1946, **2**, 114.
[2] *J. Bact.*, 1947, **54**, 363.
[3] *Proc. Soc. exp. Biol., N.Y.*, 1945, **60**, 168.
[4] *Lancet*, 1950, **2**, 46.
[5] *Science*, 1950, **111**, 254.
[6] *J. Lab. clin. Med.*, 1950, **35**, 488.
[7] *Proc. Soc. exp. Biol., N.Y.*, 1950, **74**, 93.
[8] *J. Bact.*, 1946, **51**, 95.

a mild paresis. This is because tremor is transmitted from the Betz cells in area 4 through the large fibres of the pyramidal tract. Apparently destruction of the substantia nigra or the globus pallidus removes an inhibitory influence and the abnormal movements of paralysis agitans are a consequence. It is clear that very careful selection of cases is necessary, for surgery should be reserved for the small group of cases which can be benefited by it.

Myers[1] has discussed the ideal operation, pointing out that the technique should be capable of standardization and that the treatment of patients with bilateral disturbance should be completed at one operation. Further, the operation should benefit rigidity and restriction of movement as well as tremor, and it should not lead to more impairment of function than was present pre-operatively. Its risk must be small. Several types of operation have been tried, the surgical attack being directed at the cerebral cortex, basal ganglia, or spinal cord. Cortical excision was introduced by Bucy,[2] who removed areas 4 and 6. This relieves tremor satisfactorily but causes a severe loss of power. Further, it is an operation of some severity for an elderly patient and, like other cortical excisions, may be followed by epilepsy. Myers has had success in the relief of tremor by excising the head of the caudate nucleus and division of extra-pyramidal fibres in the anterior limb of the internal capsule. Putnam[3 4] introduced section of the lateral pyramidal tract (pyramidotomy). This he performs at the 2nd cervical segment, and he finds that it relieves tremor in two-thirds of the patients. In one-third, however, the operation caused substantial weakness. Oliver[5] has modified the spinal pyramidotomy by first carrying the incision further anteriorly into the cord—with, as a consequence, some contralateral hypo-algesia—and more recently he has reported section of the whole of the lateral column of the cord.[6] This has increased the proportion of successful results and, surprisingly, has not in every case caused a hemiplegia. Ebin[7] suggests that for maximum improvement the anterior pyramidal tract on the opposite side to that on which the crossed pyramidal tract is cut should be sectioned, and he has devised a technique for doing this. He considers that the results of pyramidotomy are thus improved and that rigidity as well as tremor is diminished.

There are several points of interest in this recent work on the surgical treatment of Parkinsonism. In the first place it appears that in a small proportion of patients the disability caused by severe tremor can be reduced—though frequently at the price of a hemiparesis. Secondly, these and other methods of surgical treatment throw light upon the nerve pathways which are involved in the abnormal movements of paralysis agitans. Thirdly, it is surprising to learn that the lateral column of the cord may be sectioned in its entirety without causing a persistent hemiplegia. This finding suggests that short neurone chains may play a more important part in the transmission of impulses through the cord than has been realized in the past.

[1] *Ass. Res. Nerv. Ment. Dis. Proc.*, 1942, **21**, 602.
[2] *Arch. Neurol. Psychiat., Chicago*, 1939, **41**, 721.
[3] Ibid., 1940, **44**, 950.
[4] Ibid., 1950, **63**, 357.
[5] *Lancet*, 1949, **1**, 910.
[6] Ibid., 1950, **1**, 847.
Arch. Neurol. Psychiat., Chicago, 1949, **62**, 27.

GLUTAMIC ACID AND INTELLIGENCE

In 1944 Zimmerman and Ross[1] reported an experiment which appeared to show that maze-learning ability in the rat is significantly improved after administration of glutamic acid. Stimulated by this result, many workers have been led to study the possible effects of glutamic acid upon human intellectual capacity. Thus Zimmerman, Burgemeister, and Putnam, in a series of studies published between 1946 and 1949, have reported that the intelligence quotients of mentally retarded children and adolescents may show great increases after six months of glutamic-acid treatment. In one investigation[2] the mean increase in I.Q. for a group of 60 subnormal children on the Stanford–Binet scale was 7.7 points. Prolongation of the therapy for a second period of six months led to a further, though relatively slight, increase in mean I.Q. Zimmerman and his colleagues were therefore led to conclude that glutamic acid in some way accelerates mental function and that the greatest improvement occurs within the first six months of treatment.

Some further evidence about the effects of glutamic acid upon intellectual performance has recently been published. In a study of 85 cases of young borderline and high-grade defectives treated over a period of a year, Zimmerman and Burgemeister[3] report a gain in I.Q. of 10 points or over in 27 cases and 5–9 points in 31. Thus 68% of the defectives showed an I.Q. increase of at least 5 points. In 34% this increase brought the I.Q. up to average or low-average level. It is interesting that children presenting marked behaviour problems, or indications of organic abnormality, showed the least improvement. Quinn and Durling,[4] reporting on a smaller number of cases but using a wider variety of tests, find a comparable, though less marked, effect of glutamic acid on low-grade defectives. They noticed an average increase of 3.9 I.Q. points in 25 cases treated for six months, but found no further increase in I.Q. after a second six-months period of treatment. The general conclusion from these studies would appear to be that an increase in I.Q. from 3 to 10 points may be expected in a majority of defective children after a six-months course of glutamic-acid therapy.

A marked shortcoming of the investigations hitherto reported is the lack of satisfactory control experiments. In a recent study of the effects of repeatedly testing the same subjects with the same intelligence tests Heim and Wallace[5] have shown that mere repetition of a given test, without giving any tuition or information about results, may lead to startling increases in test scores in both normal and defective subjects. These workers report that 12 mentally deficient boys, who were not at the time undergoing any form of treatment, showed a gradual improvement in test score on 10 successive weekly performances of the same test. There appeared also to be some transfer of improvement to other tests which had not been taken previously. In the light of these findings it may be surmised that part at least of the improvement shown by individuals treated with glutamic acid can be ascribed to

[1] *Arch. Neurol. Psychiat., Chicago*, 1944, **51**, 446.
[2] Ibid., 1946, **56**, 489.
[3] *N.Y. St. J. Med.*, 1950, **50**, 693.
[4] *Amer. J. ment. Defic.*, 1950, **54**, 321.
[5] *Quart. J. exp. Psychol.*, 1949, **1**, 151; and 1950, **2**, 19.

this contingent factor of test repetition. At all events, until proper control studies are available the beneficial effects of glutamic acid upon intellectual functions must be regarded as unproved. Moreover, even if they are established, their implications for intelligence in its practical and social aspects will require well-designed clinical investigation.

DENTAL NURSES IN NEW ZEALAND

For nearly 30 years there has been in existence in New Zealand a scheme for the care of children's teeth by women who are given a two-year course of training. These "dental nurses," as they are called, should not be confused with "dental hygienists." The Dentists Act of 1921 made provision for the performance in certain circumstances of "minor dental work" in this country by unregistered persons, and, since the scaling and polishing of teeth is agreed to be minor dental work, it is done to a limited extent in Great Britain by "dental hygienists." But the filling and extraction of teeth cannot be regarded as minor dental work, and therefore in the present state of the law those operations may not be done in this country by unregistered persons. The New Zealand dental nurses, however, do fill and extract teeth, and in the early part of this year a mission consisting of five distinguished dentists visited New Zealand in order to obtain first-hand information about the training and work of the dental nurses. The members of the mission were appointed by the Minister of Health, the Secretary of State for Scotland, and the Minister of Education, and they have now submitted to those ministers a unanimous report[1] in which they express the opinion that "the training of the New Zealand school dental nurse has resulted in a high standard of technical efficiency . . . and that, subject to the staffing limitations, the dental nurse system in New Zealand meets an urgent need."

The breakdown in the school dental service in this country has caused much concern, and if it should ever be decided to amend the law so as to permit the introduction of a similar scheme here those responsible could scarcely be accused of trying to secure a dental scheme "on the cheap." The New Zealand scheme cost £322,000 for the year 1948–9, but there is little in the mission's report to indicate what results are being obtained for this expenditure. True, it records the number of extractions and fillings carried out in 1949, but it gives no information about the dental condition of the children leaving school or of adolescents, except for the statement that "one of our number had an opportunity of examining children aged 15–17 in a technical school, and the new caries rate in permanent teeth, which had been conserved for a number of years, was found to be high." The dental nurses devote a substantial amount of their time to dental health education, and yet it seems to be agreed that the incidence of dental caries in New Zealand is exceptionally high. If dental health education has really improved the dental health of New Zealand schoolchildren and adolescents it is a pity that no evidence on that point has been provided. Those responsible for the working of the scheme have secured the good will of the New Zealand dental profession. Development, however, has been so slow that even now all the children in the higher age groups do not benefit. It has therefore not been necessary to consider whether the dental nurses shall be allowed to fill and extract the teeth of adolescents and adults, but some day this issue will have to be faced. It will be interesting to see then whether the good will of the dental profession is conditional on the nurses being restricted to the care of children's teeth.

[1] *New Zealand School Dental Nurses*, Report of United Kingdom Dental Mission, 1950, H.M.S.O., London.

PULMONARY COMPLICATIONS OF PERTUSSIS

The association between whooping-cough and pulmonary collapse and bronchiectasis has been known for more than a century, but it remained for the routine use of radiography during whooping-cough to show how commonly this disease gives rise to serious, and often permanent, chest complications.[1] A number of workers have taken chest radiographs during the course of whooping-cough in order to assess the frequency of pulmonary complications and to study their subsequent course. Kohn and his colleagues[2] found that the incidence of pulmonary abnormalities detected radiologically varied directly with the severity of the disease; in severe infections the proportion of lung complications was as high as 86%. This investigation also showed quite clearly that the cause of pulmonary collapse in pertussis was not, as had often been supposed, enlargement of the hilar lymph nodes but retention of viscid secretions in the bronchi. Last year Nicholson[3] reported a series of 44 unselected cases of whooping-cough in which collapse was detected in 39, but he did not confirm previous suggestions that the high incidence was related to the severity of the disease. Elsewhere in this issue of the *Journal* Dr. A. W. Lees describes a similar investigation. Chest radiographs were taken at weekly intervals during the course of the disease in 150 consecutive cases, and those patients over the age of 1 year in whom pulmonary collapse had occurred were examined by bronchography. In all, 43% of the cases showed radiological evidence of pulmonary collapse at some stage of the illness, usually between the second and fifth weeks. The lower lobes of the lungs were most commonly affected: in fact collapse of the upper lobes and the right middle lobe was rare. This is very different from the distribution of pulmonary collapse in primary tuberculosis reported by Macpherson and Lutwyche,[4] who found that the upper lobes and right middle lobe were usually affected. Both findings therefore help to confirm the opinion that whooping-cough is the commonest cause of basal bronchiectasis and lower lobe collapse in childhood.[5 6] Lees makes the interesting observation that the collapse seldom lasted for more than a few weeks, for re-expansion had occurred in less than eight weeks from the onset of collapse in all his cases. This contrasts sharply with Nicholson's observation that 21% of patients had persistent collapse for more than a year and gives little support to the view that whooping-cough is a common precursor of chronic lower-lobe disease.

[1] *British Medical Journal*, 1949, **2**, 588.
[2] *Amer. J. Dis. Child.*, 1944, **67**, 463.
[3] *Arch. Dis. Childh.*, 1949, **24**, 29.
[4] *Thorax*, 1950, **5**, 1.
[5] Franklin, A. W., *Proc. R. Soc. Med.*, 1944, **37**, 576.
[6] Oswald, N. C., ibid., 1947, **40**, 736.
[7] Tannenberg, J., and Pinner, M., *J. thorac. Surg.*, 1942, **11**, 571.
[8] Lander, F. P. L., and Davidson, M., *Brit. J. Radiol.*, 1938, **11**, 65.
[9] —— *Thorax*, 1946, **1**, 198.
[10] Raia, A., *Amer. J. Dis. Child.*, 1938, **56**, 852.

The reason for difference between the two findings is not apparent, but it might well be due to a difference in the severity of the two epidemics.

The importance of pulmonary atelectasis in pertussis lies in its association with bronchiectasis. It is known that when pulmonary collapse takes place there is a coincidental dilatation of the bronchi in the affected portion of the lung. Experimental work has shown that in early stages this bronchial dilatation is purely mechanical, the elastic bronchi dilating to compensate for the shrinkage of the lung within the closed rigid cavity of the thorax.[7 8] For a certain time after the lung has collapsed the bronchiectasis is reversible; cases have been reported in which return to normal has taken place after collapse and bronchiectasis have been present for four to six months.[9 10] Lees's report shows that this sequence of events often takes place in the pulmonary atelectasis accompanying whooping-cough. All his cases of bronchial dilatation reverted to normal during the period of observation, the process taking somewhat longer in those with a severe degree of collapse. Probably two factors operate in rendering the bronchiectasis permanent—the duration of the collapse, and the severity of the ensuing bronchial infection. In the treatment of whooping-cough both collapse and infection must be controlled as rapidly and effectively as possible by encouraging pulmonary re-expansion and by the use of antibiotics. Lees has used artificial pneumothorax to prevent bronchial dilatation, and this method of treatment requires careful consideration.

HYPERTENSIVE AND ISCHAEMIC HEART DISEASE

Although the span of life may be little shortened in hypertension, death in patients with this complaint is most often from heart failure. The widespread arterial and arteriolo sclerosis of chronic hypertension are usually found also in the coronary arteries and their branches; and in the final affairs of the hypertensive heart it has been natural to think that myocardial ischaemia from coronary sclerosis might play the determining part. It has also been supposed that a thickening myocardium could outgrow its blood supply, thus becoming ischaemic, and that increased work for the heart muscle could bring on its premature ageing. Harrison and Wood[1] have made a fresh approach to these matters in a combined clinical and pathological study which included post-mortem injection and subsequent stereoscopic radiography of the coronary arteries, with results of great interest. Using an arbitrary clinical and electrocardiographic division they divided their cases into two groups: fifteen patients with cardiac ischaemia and evidence of angina or myocardial infarction and with various blood pressures, and twenty-seven in whom hypertension was the primary sign. Many additional clinical cases were also reviewed.

Only four of the twenty-seven hypertensive patients died without cardiac symptoms. In all the others cardiac failure had appeared, though in twelve of them death was from some other cause. In the hypertensive group there was no case in which the blood pressure was observed to drop as a result of heart failure, except terminally; and only one hypertensive patient had to be transferred later to the ischaemic group because of angina or infarction.

The pathological techniques showed that moderate atheroma did not necessarily cause narrowing of the coronary lumen, and that a paraffin section gave little or no indication of the real size of the lumen during life. In hypertension a striking feature was the enlargement of the coronary arteries, which was found to parallel the degree of cardiac hypertrophy. In the ischaemic group it was common to find in the skiagrams of coronary arteries points of narrowing which were healed recanalized thrombi, often difficult or impossible to distinguish from atheroma. This finding confirmed earlier observations of Duguid[2 3] which in themselves stimulate a fresh approach to atheroma.[4]

The axiom that a big heart fails sooner than a small one was given a fresh turn by the finding that the cardiac hypertrophy which occurred both in hypertension and in ischaemia without hypertension was to be correlated in particular with the duration of the cardiac failure.

From these studies the separation of common but distinctive diseases is made sharper, and it is evident that the weight of a hypertensive heart varies more with the duration of cardiac failure than with the height of the blood pressure. Since the size of the coronary vessels increases in step, myocardial ischaemia can no longer be accepted so often as a cause of failure.

[1] *Brit. Heart J.*, 1949, **11**, 205.
[2] *J. Path. Bact.*, 1946, **58**, 207.
[3] *Lancet*, 1949, **2**, 925.
[4] Annotation, *British Medical Journal*, 1949, **2**, 1343.

SPENS AWARDS AND CHARITY

As was foreseen in these columns[1] some heart-burning is already being caused by the distribution of the Spens merit awards to consultants, and the fact that the names of many of the recipients are already widely known makes nonsense of the secrecy that has been imposed. Not only that, but the semi-secrecy which now exists adds to the distaste felt by those who have already given expression to this in the correspondence columns of this *Journal* and of the *Lancet*.

In a letter this week Dr. Katharine Lloyd-Williams, who is the dean of the Royal Free Hospital School of Medicine, informs us that some consultants are refusing to accept the awards that have been made. She makes the excellent suggestion that, instead of sending this money back to the place where it comes from, those consultants who reject these payments should instead make them over to one of the medical charities. This proposal receives the support of no less a person than Lord Webb-Johnson,[2] who points out that if the subscriber to a charity enters into a seven-years covenant the income-tax can be recovered by the charity in whose favour the covenant is drawn.

Consultants and specialists generally have accepted the Spens awards as a method of supplementing the income of those working in the National Health Service. Those who have accepted the majority decision but reject the principle may nevertheless feel justified in devoting the money to the most worthy cause of medical charity. They will, however, in later years be faced with the dilemma of what to do with the pension which is due to them on the basis of the money awarded.

[1] *British Medical Journal*, 1948, **1**, 1140; 1949, **2**, 745, 1400; 1950, **1**, 295.
[2] *Lancet*, November 11, 1950, p. 540.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

ADDISON'S DISEASE

BY

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Thomas Addison, of Guy's, when he read his paper before the South London Medical Society in 1849 (at the age of 56), or published his more significant monograph *On the Constitutional and Local Effects of Disease of the Suprarenal Capsules* in 1855, could hardly have fully realized that he had founded the science of clinical endocrinology or that the isolation and synthesis of the many vital hormones secreted by the adrenal gland would occupy some of the best biochemists of the New and the Old World in the middle of the twentieth century. This brief revision article, however, is limited to the disease of adrenal insufficiency, so appropriately called Addison's disease, and so adequately described in clinical and pathological terms by Addison in 1855.

As to the pathology of Addison's eleven cases, six showed destruction of the adrenal glands by tuberculosis and three by secondary carcinoma, one only showed atrophy and fibrosis, and one a carcinomatous nodule blocking the adrenal vein. A more extensive series of cases shows bilateral tuberculosis to be the cause in some 70% of cases, idiopathic atrophy or necrosis in 25%, and malignant destruction and other causes to be comparatively rare. Pulmonary tuberculosis is only rarely complicated by Addison's disease; but glandular or bony or genital tuberculosis not infrequently has been present some years previously and may be clinically healed before the onset of adrenal insufficiency. There is no clue to the cause of the non-tuberculous atrophy, which is therefore called idiopathic, but it is not unreasonable to postulate a virus infection comparable to the influence of the virus of mumps on the testicles.

Essential Hormones Secreted by Adrenal Cortex

It is generally held that the practitioner is not much concerned with physiology and biochemistry, and I would agree that his busy life limits his interest in the more technical and abstract aspects of these subjects. Nevertheless, in endocrinology, if not so much in other branches of medicine, the fundamentals of these subjects throw considerable light on symptomatology, diagnosis, and treatment. I will therefore consider briefly the essential hormones secreted by the adrenal cortex, the medulla playing little or no part in the deficiency disease of the adrenals.

1. Deoxycortone, or "sodium hormone."—This controls the plasma concentration and excretion of sodium, chloride, and potassium. In the adrenalectomized animal, or the patient with Addison's disease, there is increased urinary excretion of sodium and chloride and retention of potassium, so that the plasma sodium and chloride concentrations tend to be low and the plasma potassium tends to be high. The injection of deoxycortone corrects these changes in mineral metabolism.

2. The corticosterone (11-oxysteroid) group or diabetogenic anti-insulin hormones.—The adrenalectomized animal, or the patient with Addison's disease, manifests a tendency to hypoglycaemia, more evident under conditions of fasting or stress, and in contrast a patient with an adrenal tumour secreting an excess of 11-oxysteroids, as in Cushing's syndrome, may show clinical diabetes mellitus.

3. The adrenals secrete androgens, oestrogens, and progesterone, which hormones may be grouped together as sex hormones.

4. When these groups of hormones have been extracted there remains an amorphous fraction, which is more potent weight for weight than the crystalline hormones in maintaining the life of adrenalectomized animals and which also favourably influences renal function.

5. Knowledge is accumulating about an adrenal fat-controlling hormone, excess of which causes a general deposition of fat in the tissue; in contrast the tissues of adrenalectomized animals are almost devoid of fat.

6. Pigment-controlling hormone which seems to have some co-ordinating action with pituitary, in so far as the excessive deposition of melanin in the skin is very marked in Addison's disease, but is slight or absent in Simmonds's disease, in which, however, the adrenal cortex is atrophied and is functioning poorly as judged by carbohydrate and mineral metabolism abnormalities. It is difficult to study the pigment factor in adrenalectomized animals.

Clinical Manifestations of Addison's Disease

The main features are muscular weakness and tendency to fatigue, loss of appetite, loss of weight, low blood pressure, and pigmentation of the skin and mucous membranes. Anorexia may be particularly marked with fatty foods, and may be associated with nausea, vomiting, and intermittent diarrhoea. Abdominal pain and colic are met with

Extreme pigmentation of the hands in a girl of 18 with acute Addison's disease, showing excessive deposition of melanin especially on the dorsal aspect of the finger-joints. (This illustration, from the author's *Major Endocrine Disorders*, is reproduced by permission of the Oxford University Press.)

and the diaphragm may be irritated by the underlying diseased adrenal, with resulting costal or referred shoulder pain. Hiccup, yawning, conjunctivitis, grimaces, involuntary cries, negativism, contrariness, and apathy constitute an interesting group of associated symptoms of clinical and diagnostic significance. Sensitivity to cold, with curling up under the bedclothes, and a subnormal temperature are features which may be associated with a low basal

metabolism. Menstruation may be quite normal, and pregnancy may occur, but amenorrhoea and impotence are met with.

Hypoglycaemic symptoms may or may not be present, but in some patients hypoglycaemic coma can come on with great suddenness and lead to death if undiagnosed. The pigment is an increase of the normal melanin in the basal layers of the epidermis, and is found in the skin exposed to air or sunshine, for example, on the face and backs of hands (see Figure), and to pressure or friction, for example, in the axillae, groin, and under the waistband. Pigment may also be present on the gums and lips and in the buccal and anal mucous membranes. In a fair patient, who in health tends to go red rather than brown in summer, pigmentation may be slight or absent. The same is true when the adrenal insufficiency is of acute onset. Pigmentation may occasionally be of leucodermic type, as in one of Addison's patients, and in a case of mine that came to necropsy. This is probably explained by adrenal insufficiency being superimposed on, and accentuating, a previous or coincident tendency to leucoderma.

Diagnosis

Addison's disease may occur at any age, but is very rare before puberty or after 60. It is most frequent in the second and third decades. Diagnosis is not difficult if the above symptomatology is met with, but dramatic missed diagnoses may be seen if the disease is not kept in mind. Thus in one teaching hospital a man aged 36 was operated upon for a supposed perforated duodenal ulcer and nothing was found. At necropsy both suprarenal glands were seen to be destroyed by tuberculosis and pigment was obvious on the skin and buccal mucous membranes. In crisis the picture of Addison's disease closely resembles surgical shock, and it was this resemblance that stimulated Loeb to the discovery of the salt loss in Addison's disease. An opposite but less serious error was the diagnosis of Addison's disease in a case of normal early pregnancy associated with physiological pigmentation in a dark-skinned person and some vomiting and malaise. This was more easily understandable, since there is an extra demand upon the adrenal cortex in pregnancy, and some cases of Addison's disease are first revealed by a pregnancy, and may temporarily clear up for a while after it.

Addison's disease may be very acute and severe and quickly fatal, or may be mild and chronic, one such patient being alive and well after eight years, the only treatment being moderate amounts of salt by mouth. Such mild chronic cases may nevertheless be associated with deep and intense generalized pigmentation. In a crisis, not only is the blood pressure very low and the pulse almost imperceptible, but there is considerable haemoconcentration and collapse of the veins, which latter may be very difficult to enter with a needle, making venous blood difficult to withdraw. In the more chronic phases blood pressure may be normal, or occasionally high, if there has been a pre-existing hypertension. Similarly the fasting blood sugar may be normal, though it tends to fall in crisis.

In Simmonds's disease there is also weakness, anorexia, loss of weight, low blood pressure, low blood sugar, and subnormal temperature. Pigmentation is absent or mild and patchy. Amenorrhoea in Simmonds's disease is almost invariable, and complete loss of pubic and axillary hair is the rule, to which, however, there are definite exceptions. Bradycardia and a pronounced lowering of the basal metabolic rate in the absence of crisis favour a diagnosis of Simmonds's disease. If the condition has followed parturition associated with haemorrhage or infection, or if there is evidence of a craniopharyngioma or chromophobe adenoma of the pituitary, the diagnosis is Simmonds's disease and not Addison's disease. For all practical purposes, and excluding racial pigmentation, mucous membrane pigmentation is pathognomonic of Addison's disease, but is by no means an essential feature.

As to biochemical data, normal plasma or serum values are: sodium, 320–350 mg. per 100 ml. (or 141 milli-equivalents); chloride, 355 mg. expressed as Cl or 585 mg. expressed as NaCl per 100 ml. (or 100 milli-equivalents expressed either as Cl or NaCl); potassium, 18 to 20 mg. per 100 ml. (or 5 milli-equivalents). A milli-equivalent is milligrams per litre, divided by the atomic weight for monovalent elements. In Addison's disease, particularly in crisis, the sodium may be, for example, 290 mg., the chloride (as NaCl) 485 mg., and the potassium 28 mg. per 100 ml. In the more chronic phases a normal mineral chemistry does not exclude Addison's disease and the sodium values are more likely to be lowered than the chloride values. As to the potassium, this is elevated only in severe adrenal insufficiency. The blood urea is raised appreciably in severe insufficiency or crisis.

The Kepler test is a quotient arrived at by the study of blood and urine chloride and urea concentrations and water excretion. In Addison's disease the quotient is less than 30 and usually less than 15. (Blood for estimation of minerals must be taken into a special "pyrex" tube and the serum separated immediately after clotting; it is not essential to collect under liquid paraffin.)

The blood count may show a leucopenia, relative lymphocytosis, and eosinophilia. This eosinophilia is rarely depressed more than 30% by the injection of 0.3 mg. of adrenaline subcutaneously, or 25 mg. of A.C.T.H. intramuscularly, and is usually not affected at all by such injections, there being no adrenal cortex left that can respond. The measurement is made before and four hours after the injection, and is suggested by Thorn as an additional diagnostic test, patients with normal adrenals showing a consistent 50% fall in eosinophils. The sedimentation rate is often raised whatever the pathological lesion of the adrenals may be. The urinary 17-ketosteroids are decreased, particularly in women.

Treatment

The logical treatment of adrenal insufficiency is replacement therapy with an adrenal extract which contains all the essential hormones, and such therapy must be continued for life as with insulin for diabetes mellitus. Unfortunately available extracts are neither comprehensive in their content nor concentrated enough to make therapy completely adequate. Nevertheless, cortical extract can be used with good clinical results, the average patient requiring some 10 ml. daily, injected intramuscularly. With more severe insufficiency as much as 30 ml. is required daily. These extracts have some action upon both mineral and carbohydrate metabolism. Occasionally a patient reacts allergically to such injections, either locally or generally, and continued therapy is not possible. Where there is some pain at the site of injection, the addition of 0.2 ml. of 2% procaine hydrochloride to the contents of the syringe is helpful.

Deoxycortone acetate influences only mineral metabolism and does not correct hypoglycaemia, at least directly. Nevertheless, by increasing well-being and appetite it may be useful even in this direction also. It is prepared in ampoules of 5 mg. and 10 mg. in 1 ml. of oily solution. The average patient requires 5 mg. daily injected intramuscularly, and

because of the small bulk patients prefer this to cortical extracts. Further, deoxycortone can be implanted subcutaneously, one tablet of 100 mg. being used for each 1 mg. of injected material. Thus the average patient receiving 5 mg. daily would have implanted 500 mg. of deoxycortone tablets (five tablets of 100 mg. each). Before calculating this dosage it is advisable to maintain the patient for several weeks on injections, as the ultimate daily maintenance dosage may be appreciably less than the initial dosage.

As the effects of overdosage are severe and potentially fatal, I subtract 100 mg. from my calculated implantation dose, and for further safety I rarely do an initial implantation of more than 300 mg. The implantation calculations I have given are the ones I initially recommended, but are only half of the equivalents given by an American authority.

The effects of overdosage are seen both with the injection method and with the implantation method, but the former is much easier to correct than the latter, which necessitates removal of tablets. Overdosage leads to excessive retention of fluid and sodium, with increased excretion of potassium and low potassium serum concentration, resulting in weakness and paralysis of muscles, including the cardiac muscle. Other characteristic manifestations are superficial oedema of face and limbs, crepitations in the lungs, and enlargement of the heart, with or without pericardial effusion. The oedema, however, may not be conspicuous, and the excessive weakness or paralysis may be wrongly regarded as due to inadequate treatment. The blood chemistry may be deceptive in that the sodium and chloride may be normal, but the serum potassium is always low—for example, 12 mg. per 100 ml. Hypertension may be present initially with excessive fluid retention, but with cardiac failure this gives place to hypotension. Apart from the oedema of the cardiac muscle, multiple foci of necrosis in the heart have been found at necropsy. Electrocardiographic changes, with low serum potassium, are low-voltage QRS complexes, lowering or inversion of the T waves, depression of the S–T segment, and prolongation of the QRS interval. Occasionally some patients show a more insidious chronic dry hypertension with this treatment, but in the absence of the other features this is not usually important and may tend to correct itself. (Such low potassium concentrations are also met with in diabetic coma treated with intravenous salines and glucose, in infantile diarrhoea, and in surgical operations where there have been diarrhoea, intestinal drainage, and/or excessive intravenous saline.)

The best treatment of overdosage in Addison's disease is removal of the implanted tablets, but as a preliminary emergency measure 100 ml. of 2% potassium chloride may be injected intravenously. If the dosage is properly calculated, however, implantation therapy is excellent, and since the effects last some eight months many patients prefer it to all other methods of treatment. As the effect of therapy wears off the administration of salt by mouth may permit the postponement of further implantation from the sixth to the tenth month. Salt is also given by mouth without any other therapy in mild cases of Addison's disease. The dosage is up to 12 g. daily (three teaspoonfuls) in divided doses in a tumblerful of water or lime juice, or with porridge or potatoes. A mixture of sodium chloride, phosphate, citrate, and bicarbonate may prove more palatable. Sodium chloride in 1-g. capsules can also be obtained. Additional salt should be given with caution if deoxycortone is also used, for fear of excessive water and salt retention.

Such overdosage effects of deoxycortone as described above are not usually met with if cortical extracts are used, especially if the daily dose of the latter is less than 20 ml. In the U.S.A. a concentrated lipoid-extract of hog's adrenals has been prepared which is five times as potent as an aqueous extract, particularly in regard to the effect on carbohydrate metabolism. The extract is not yet available in this country. Linguets of adrenal cortical extracts for dissolving under the tongue, as prepared for some American investigators, have proved adequate for prolonged therapy, but those available to me have not proved sufficiently constant in action. Testosterone or methyl testosterone is indicated where the urinary 17-ketosteroids are less than 5 mg. a day, but if implanted the augmentation thereby of the sodium and fluid retention of deoxycortone must be reckoned with. In crisis, or in the acute phase of adrenal insufficiency, treatment differs from the more chronic phase only in its intensity and the advisability of using both cortical extract and deoxycortone. Intravenous saline is called for if the patient has been allowed to become very collapsed, and it is often necessary to cut down on a vein. If severe hypoglycaemia is suspected—and this is more likely in a patient who has been treated previously with deoxycortone and not cortical extract—intravenous glucose is necessary.

Course and Prognosis

Even if adequately treated, as judged by biochemical data, the more severe cases of Addison's disease lead a precariously balanced existence, and are liable to go into crisis, with or without a precipitating cause—for example, infection, trauma, strain—and to have phases of hypoglycaemia, sometimes acute and dramatic. They tend to lose weight and body fat over a period of years, and the pubic and axillary hair may become thinned. Apathy and inertia are not infrequent, and there is often a sensitivity to cold and infection. Nevertheless, one of my patients had two successful pregnancies under treatment, and is a good mother to the children and an efficient wife. Another seemed to have a sustained remission during her climacteric, and then partially relapsed again.

BRONCHOSPIROMETRY

SEMON LECTURE BY DR. PAUL FRENCKNER

The annual Semon Lecture was delivered at the Royal Society of Medicine on November 2 by Dr. PAUL FRENCKNER, of the Karolinska Institutet, Stockholm. His subject was "The Development and Present Use of Bronchospirometry." Dr. E. R. BOLAND, Dean of the Faculty of Medicine, London University, was in the chair.

Dr. FRENCKNER began with a tribute to Sir Felix Semon, whom he described as one of the greatest laryngologists of all time, with whose work and discoveries, he said, he had come into contact in his own first laryngological studies, on paralysis of the vocal cord, 25 years ago.

Dr. Frenckner described his first experiments in 1929 in what he called bronchial catheterization. His purpose was to work out a method of clinical examination with which it would be possible to judge the function of each lung separately, in the same manner as it was possible to form an opinion on each kidney by ureteral catheterization. By bronchial catheterization was meant the passing of a tubular instrument, flexible or rigid, into a predetermined bronchus, an airtight closure between the bronchial wall and the instrument being obtained by means of a special fixture at its distal end, so that it was possible to transmit to or from the area of distribution of the airway in question a gaseous or fluid substance for diagnostic or therapeutic purposes. In association with Jacobaeus and others in Sweden the concept of bronchospirometry was created. Various instruments had been used during the development of the investigation, but the work took a big step forward with the introduction of Carlens's

double catheter, which was made of rubber of about the same rigidity as the ordinary urethral catheter. This was introduced, without fluoroscopy, under mirror guidance over a curved metal stylet.

Investigation of Miners' Lungs

The lecturer went on to describe an investigation on the labourers at certain gold and copper mines, who were much exposed to arsenic fumes and sulphur dioxide. Despite protective arrangements, these workers showed pronounced atrophy of the respiratory tract mucous membrane from the nose to the bronchi. The object of the spirometric examination was to ascertain whether there was any disturbance of pulmonary function which could be ascribed to emphysema or epithelial damage, and, if so, whether both lungs showed the same degree of impaired function. Dr. Frenckner gave an account of the results from the 75 cases so far examined.

Carlens's rubber catheter was introduced under local analgesia and attached to an oxygen-filled double spirometer. The recording went on for eight minutes while the subject breathed with maximal inspiration and expiration; forced breathing followed for a quarter or half a minute, and then the residual air was determined. The volumetric values of particular interest were those indicating total capacity, vital capacity, and oxygen consumption. Variations in the total capacity for each lung were often considerable. The average value in the cases taken was 2,600 ml. for the right lung and 2,400 for the left, but this average was found in only a small percentage of the cases, and there were deviations of as much as 500 ml. above or below. Impaired function of one or both lungs was demonstrated in a number of cases.

The vital capacity values were on the average very much below normal, and some of the deviations were considerable. The oxygen absorption was also noted, and, in the cases where it was low on the spirometer reading, bronchoscopy showed the mucous membrane to be extremely atrophic, although, owing to some other observations, he was unwilling to admit at present more than a suspicion that atrophy and poor oxygen consumption might be related. His general conclusion was that the recorded values for oxygen consumption might possibly indicate decreased lung function, which in certain of the cases was considerably more pronounced in one lung than in the other. It was possible that this decreased oxygen absorption might be due to epithelial damage.

Exchange of Respiratory Gases

Estimation of the respiratory gas exchange had been made with the help of the "residual quotient," the "equilibrium quotient," and the "ventilation equivalent" at rest and on forced breathing, in addition to oxygen consumption. The residual quotient $\left(\frac{\text{residual air}}{\text{total lung capacity}}\right)$ showed high values throughout, indicating a decreased lung function with poor emptying ability. In some few cases the difference between right and left lungs was marked, probably indicating unilateral damage. The most likely cause of the impaired function was emphysema, but epithelial damage caused by poisonous gases could not be excluded.

The equilibrium quotient $\left(\frac{\text{supplemental air + residual air}}{\text{total lung capacity}}\right)$ in the majority of cases was within normal limits, the increased residual air values being compensated by very low values for the supplemental air. The ventilation equivalent in this investigation had been calculated according to the formula $\frac{\text{minute ventilation}}{\text{oxygen consumption/min.}} \times 10$, and should be the most important factor in estimating the condition of the alveolar epithelium. The values obtained indicated that the alveolar epithelium had been damaged and that the damage had affected the right and left lungs unequally.

Routine Examination in Lung Disease

Dr. Frenckner said that bronchospirometry was also useful in the routine investigation of certain lung diseases. It was often helpful to be able to estimate the oxygen consumption, and to determine the residual quotient and ventilation equivalent, of each lung separately, particularly in cases where operation or irreversible collapse therapy was likely to be performed.

Finally the lecturer spoke of a new method of recording which would permit of a more careful analysis of the breathing phases. The ingoing and outgoing air from each lung was passed over a small sensitive antenna made of the finest platinum wire. This wire was in an electric circuit, and, on being cooled by the passage of air, variations in voltage took place, and were registered by an oscillograph. Interesting details were brought out in the curves obtained. Delay in one lung might be recorded with precision to 0.1 sec. Inhalation and exhalation gave typical recordings, and certain diseases such as asthma appeared to have characteristic curves.

Dr. Frenckner said that he himself was not a lung physiologist; his purpose was to find a method of clinical examination which would make it possible to appraise the functional capacity of the lungs under normal and pathological conditions. Apparatus was still far from perfect and needed to be critically tested and improved.

The lecture, which was followed by a film, was greatly appreciated by the large audience of laryngologists and others assembled.

OPENING OF THE NEW LABORATORIES OF THE PNEUMOCONIOSIS RESEARCH UNIT

[By a Special Correspondent]

The new research laboratories of the Medical Research Council's Pneumoconiosis Research Unit at Llandough Hospital, near Cardiff, were opened by Mr. Herbert Morrison, the Lord President of the Council, on October 28.

This Unit was set up by the Medical Research Council in 1945 at the request of the Ministry of Fuel and Power to investigate coal-miners' pneumoconiosis. Dr. C. M. Fletcher was appointed director of the Unit, and the staff now consists of 12 medical and 8 non-medical scientists, with their technical and administrative assistants.

The new building, designed by Mr. A. Steele, A.R.I.B.A.—at the time chief architect to the Cardiff Corporation—and constructed under the supervision of Mr. G. Griffiths, A.R.I.B.A., houses the whole Unit with the exception of a pathologist working under Professor J. Gough in the Department of Pathology of the Welsh National School of Medicine. It is a long single-story building with a flat roof, connected to Llandough Hospital by a covered way. The windows are arranged in long continuous strips extending over several rooms to give the maximum amount of light. The building comprises 37 laboratories, 18 offices, *x*-ray and out-patient departments, animal quarters, dark-rooms, workshops, stores, garage, kitchen and refectory, and a large conference room also used as a library. There are some 90 rooms in all. Both sides of the north corridor are devoted to laboratories for the study of the concentration and composition of airborne dusts by chemical, physicochemical, and petrological methods. There is also a large laboratory containing a wind tunnel in which artificial dust clouds may be generated for the testing of dust-sampling apparatus. The physiological laboratories are at the west end of the south corridor with the administrative block and conference room in the centre, and the offices of the epidemiological section are at the eastern end of the same corridor. There are five basement rooms containing a photographic department, a constant-temperature store-room, and a calorifier which is supplied with steam heat by the hospital.

The Unit also possesses a mobile *x*-ray van and an office van for use in radiological surveys at mines. These are being used at present for a large-scale survey of pneumoconiosis and tuberculosis in the Little Rhondda Valley (Rhondda Fach Scheme).

Research Programme

The following problems are at present being investigated by the Pneumoconiosis Research Unit:

1. The natural history of pneumoconiosis, and in particular the effect of further dust exposure on its progression. This has been studied by the re-examination of men who have been examined by others in the past. It is now being studied by following up men who have been examined in the course of radiological surveys in the field. The knowledge obtained in this way should be of use in preventing the progression of pneumoconiosis, by means of periodic *x*-ray examinations.

2. The social consequences of pneumoconiosis and problems arising in the re-employment in other industries of men disabled by the disease.

3. Methods of medical treatment and rehabilitation, including in the special case of silicosis the use of aluminium therapy.

4. Methods of improving the reliability and accuracy of the radiological diagnosis of pneumoconiosis.

5. The nature of the disturbance of lung function which causes dyspnoea on exertion in cases of pneumoconiosis and other related disorders.

6. The effect of exposure of animals to dusts of various compositions, including samples of airborne dust obtained from the mines.

7. The measurement of the concentration and composition of airborne dusts in mines in Wales and other parts of Great Britain and their relation to the incidence of disease at the same mine as estimated by *x*-ray surveys.

8. The relationship between pneumoconiosis and tuberculosis. This is at present being investigated by submitting the whole population of part of the Rhondda Valley to radiological examination in order to find and isolate all infective cases of tuberculosis. The effect on the development of pneumoconiosis in the valley will be observed.

The Inaugural Ceremony

In welcoming the Lord President, Dr. Fletcher paid tribute to the assistance he and his colleagues had received from many quarters—from the Welsh National School of Medicine, from the University of South Wales and Monmouthshire, from the miners and their leaders, and from officials of the National Coal Board at every level. He paid special tribute to Professor Gough's pathological work, to the Pneumoconiosis Medical Panels for allowing the Unit access to their medical and radiological records, and to the United Cardiff Hospitals for the beds at Llandough. He then gave a brief account of the work of the Unit.

The Lord President, in declaring the new building open, spoke of the serious incidence of the disease and of the steps which were being taken to overcome it. He said that coal-mining had always been regarded as a hazardous occupation, but rather from the point of view of accidents than from the fear of disease. In the past the coal dust which the miners inhaled had been considered harmless to their lungs, and it was not until about 30 years ago that attention had been drawn to the existence of a serious lung condition among South Wales miners, now known as pneumoconiosis.

Mr. Morrison said that the disease now constituted almost as great a threat to the industry as accidents. During the last 20 years 36,000 miners had been certified as having pneumoconiosis, and during the same period the number of fatal and serious accidents had been 75,000. He pointed out that it was necessary to do everything possible to eliminate the disease, for three reasons: first, to alleviate the suffering which it causes; secondly, because the country could not afford to lose 3,000–4,000 miners a year; and, thirdly, because of the cost of compensation. The cost of research was equal to only one-thirtieth of the annual cost of compensation. He explained that the problem was being dealt with in two ways—by medical research and by dust suppression in the mines—and he ended his speech by declaring that the Government would do all that it could to safeguard those who worked in the mines.

Mr. Alfred Robens, M.P., Parliamentary Secretary to the Ministry of Fuel and Power, said that he had frequently visited the Pneumoconiosis Research Unit, and was greatly impressed by the enthusiasm with which Dr. Fletcher and his team were tackling the problem. Mr. Robens emphasized the need for periodic examinations of all underground workers. He hoped to see at least a pilot scheme introduced in the near future.

Mr. Gilbert Shepherd, chairman of the board of governors of the United Cardiff Hospitals, proposing a vote of thanks to the Lord President and Mr. Robens, stated that his board recognized the urgent necessity of providing hospital beds for research into coal-miners' pneumoconiosis despite the present shortage of beds.

Mr. Alfred Davies, president of the National Union of Mineworkers, South Wales area, said that since last February alone his union had paid out death benefits to the dependants of between 170 and 180 pneumoconiosis victims in South Wales. He was pleased at what had already been done, but he was dissatisfied that there was still no special treatment centre for sufferers from pneumoconiosis in the area.

After cutting the tape across the entrance of the new building, the Lord President and the visitors to the Unit made a tour of the building, where a number of demonstrations had been prepared. In a small museum there was a demonstration of the standard films now used in the Pneumoconiosis Research Unit to improve the accuracy of radiological diagnosis. There was also a demonstration of sections prepared by Professor Gough and Mr. Wentworth, of the Department of Pathology, Welsh National School of Medicine, and charts indicating some of the main lines of research carried out by the Unit. An apparatus for the simultaneous recording of a spirogram and tracings of thoracic and diaphragmatic movement was on view in the *x*-ray department, together with the results of some experimental investigations into the definition obtainable by the various types of miniature radiographic technique. On the physiological side, methods of measuring lung volume, speed of gas replacement in the lungs, and maximum breathing capacity were on view. The maximum-breathing-capacity machine was being worked by an "artificial lung" designed to deliver a known "respiratory" volume with a respiratory pattern similar to that of a normal man. The epidemiological section displayed the results of radiological field surveys together with an apparatus for the rapid counting of Findex cards. The various instruments used for underground dust sampling were displayed in the dust-tunnel room, together with some samples of dust which were being submitted to analysis. In the animal house was shown apparatus for the exposure of small animals to constant concentrations of various dusts over long periods.

Finally, the visitors saw the ward in Llandough Hospital, where the Lord President inspected the products of occupational therapy and spoke to the patients, some of whom were carrying out remedial exercises. The party then adjourned to tea at Llandough Hospital, kindly provided by the board of governors of the United Cardiff Hospitals.

Reports of Societies

INDUSTRIAL HEALTH IN THE SERVICES

Three short communications on industrial health in the Services were given on November 2 at a meeting of the Services Section of the Royal Society of Medicine, Sir H. LETHEBY TIDY presiding.

Occupational Health in the Royal Navy

Mr. A. D. FREDERICK discussed occupational health risks to which Service and civil personnel in the Royal Navy and in Admiralty establishments were exposed. He mentioned, for example, the health risks attending the operations undertaken for the preservation of ships before passing them into reserve. Other risks attended the care and maintenance of refrigerators and cooling machinery operating on methyl chloride and of fire-fighting equipment containing carbon dioxide and other substances. Painting was carried out on a very large scale, by both civilian employees and Service personnel. Application by brush was now being supplanted by the use of compressed-air sprays, which had the advantage of allowing otherwise inaccessible places to be reached comparatively easily, but their operation in confined spaces meant an added health

R. D. PASSEY AND L. DMOCHOWSKI: FREEZE-DRYING OF MOUSE TUMOURS

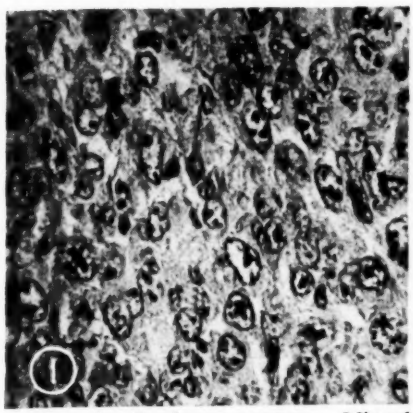


FIG. 1.—Crocker sarcoma. Minced tumour tissue before freezing. H. and E. (× 500.)

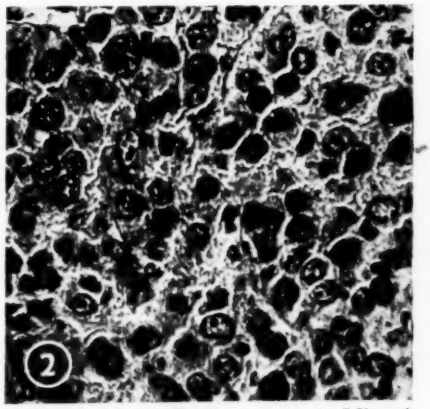


FIG. 2.—Same Crocker sarcoma. Minced tumour tissue suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 22 days; desiccated; reconstituted in equal quantities of 1:500 neutral solution of cysteine and 5.3% glucose. H. and E. (× 500.)

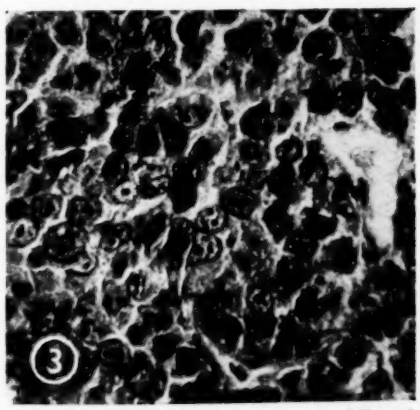
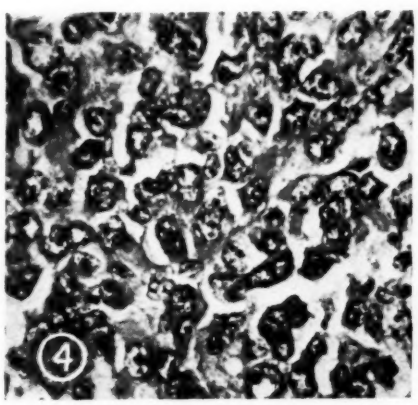
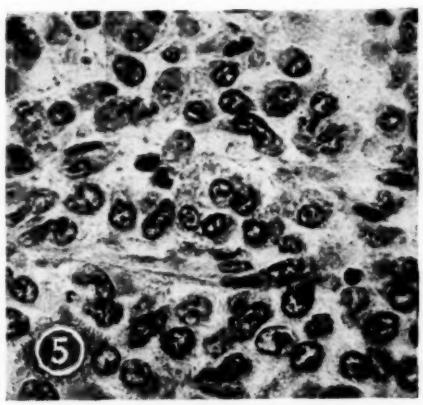
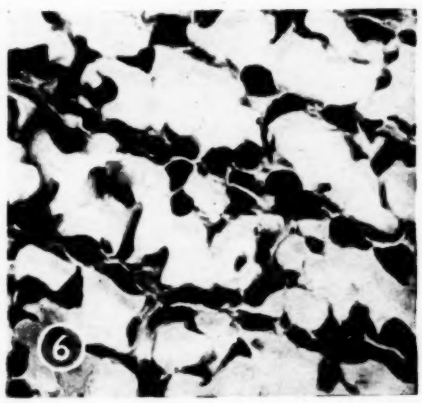
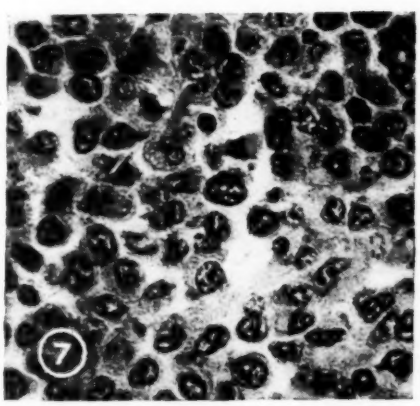


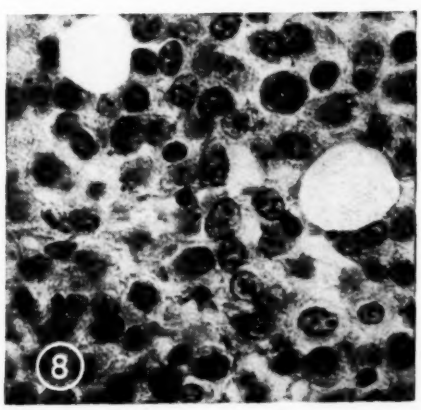
FIG. 3.—Same Crocker sarcoma. Minced tumour tissue, suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 22 days; desiccated; reconstituted in cysteine and glucose. Some damaged cells seen. H. and E. (× 500.)











FIGS. 4–8.—37S sarcoma. Minced tumour tissue. H. and E. (× 500.)

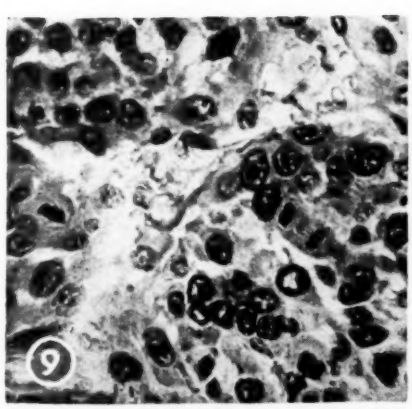
FIG. 4.—Before freezing.

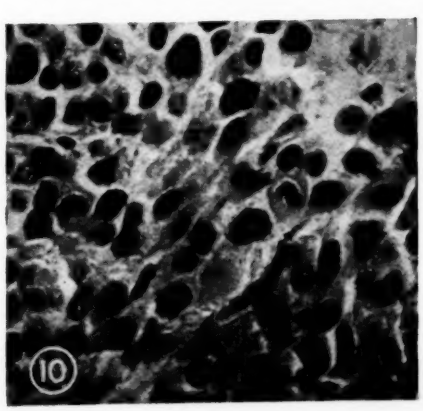
FIG. 5.—Suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 18 days.

FIG. 6.—Suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 18 days; desiccated.

FIG. 7.—Suspension in 5.3% glucose; frozen at −79° C. for 18 days; desiccated; reconstituted in 5.3% glucose

FIG. 8.—Suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 18 days; desiccated; reconstituted in 5.3% glucose. Some damaged cells seen.





FIGS. 9–10.—C48 (I.C.R.F.) methylcholanthrene-induced sarcoma. H. and E. (× 500.)

FIG. 9.—Tumour tissue before freezing.

FIG. 10.—Minced tumour tissue; suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 51 days; desiccated; reconstituted in cysteine.

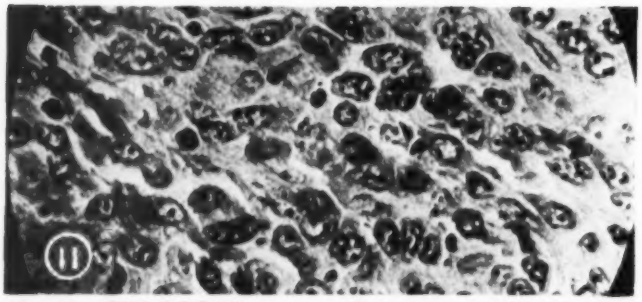


FIG. 11.—C3H (I.C.R.F.) sarcoma. Tumour tissue before freezing. H. and E. (× 500.)

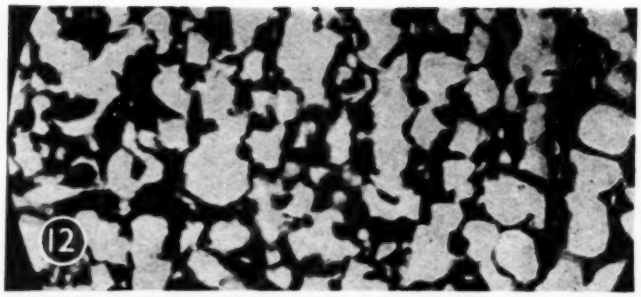


FIG. 12.—Same C3H (I.C.R.F.) sarcoma. Minced tumour tissue; suspended in 5.3% glucose frozen at −79° C. for 29 days; desiccated. H. and E. (× 500.)

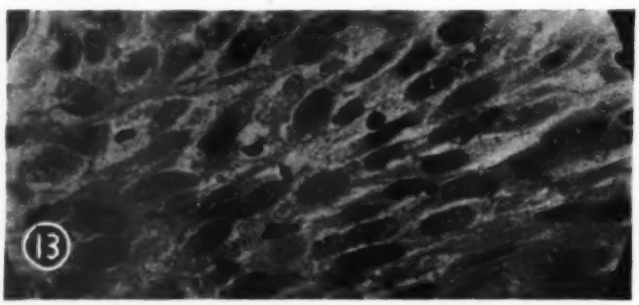


FIG. 13.—Same C3H (I.C.R.F.) sarcoma. Minced tumour tissue; suspended in 5.3% glucose; frozen at −79° C. for 29 days; desiccated; reconstituted in 5.3% glucose. H. and E. (× 500.)

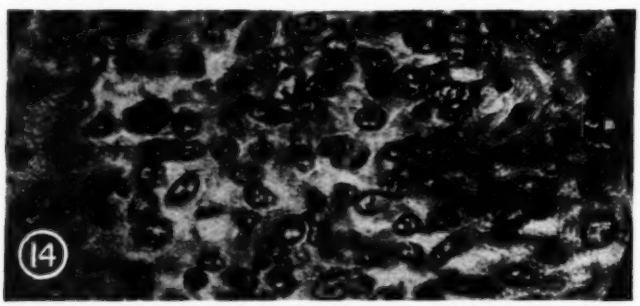


FIG. 14.—Same C3H (I.C.R.F.) sarcoma. Minced tumour tissue; suspended in 5.3% glucose; frozen at −79° C. for 29 days; desiccated; reconstituted in 5.3% glucose; centrifuged for two minutes at 7,000 times gravity. Sediment. H. and E. (× 500.)

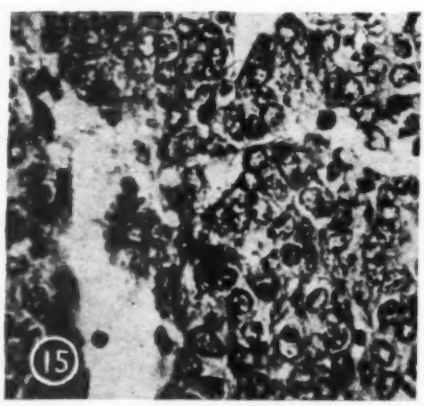


FIG. 15.—C3H transplantable breast carcinoma tissue before freezing. H. and E. (× 500.)

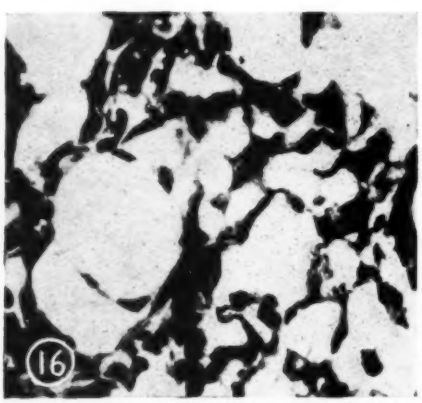


FIG. 16.—Same C3H transplantable breast carcinoma. Minced tumour tissue; suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 38 days; desiccated. H. and E. (× 500.)

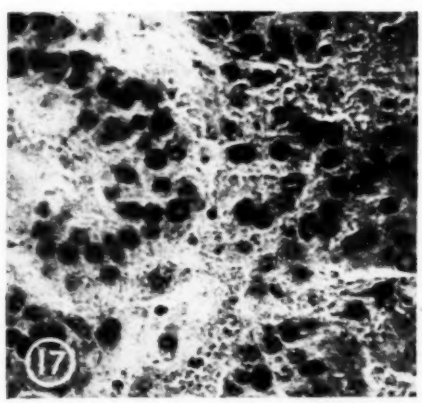


FIG. 17.—Same C3H transplantable breast carcinoma. Minced tumour tissue; suspension in 5.3% glucose; frozen in CO_2 at −79° C. for 38 days; desiccated; reconstituted in cysteine and glucose; centrifuged for three minutes at 7,000 times gravity. Sediment. Damaged cells seen. H. and E. (× 500.)

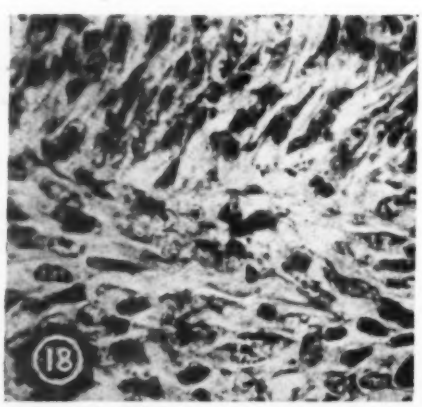


FIG. 18.—RIII (No. 4) sarcoma; not frozen and not desiccated. Control. H. and E. (× 500.)

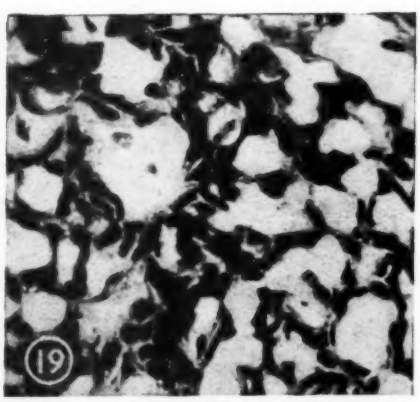


FIG. 19.—Same RIII (No. 4) sarcoma. Frozen in 5.3% glucose at −79° C. for 87 days; desiccated for 3½ hours. H. and E. (× 500.)

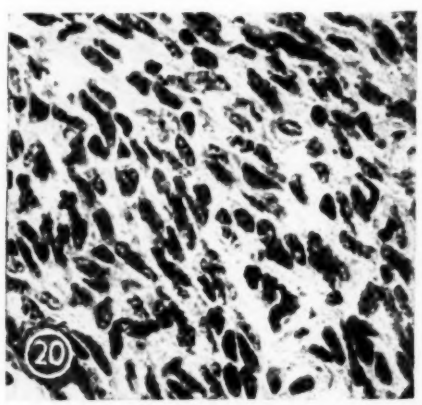


FIG. 20.—Same RIII (No. 4) sarcoma. Frozen in 5.3% glucose at −79° C. for 87 days; desiccated for 3½ hours; reconstituted in 5.3% glucose. H. and E. (× 500.)

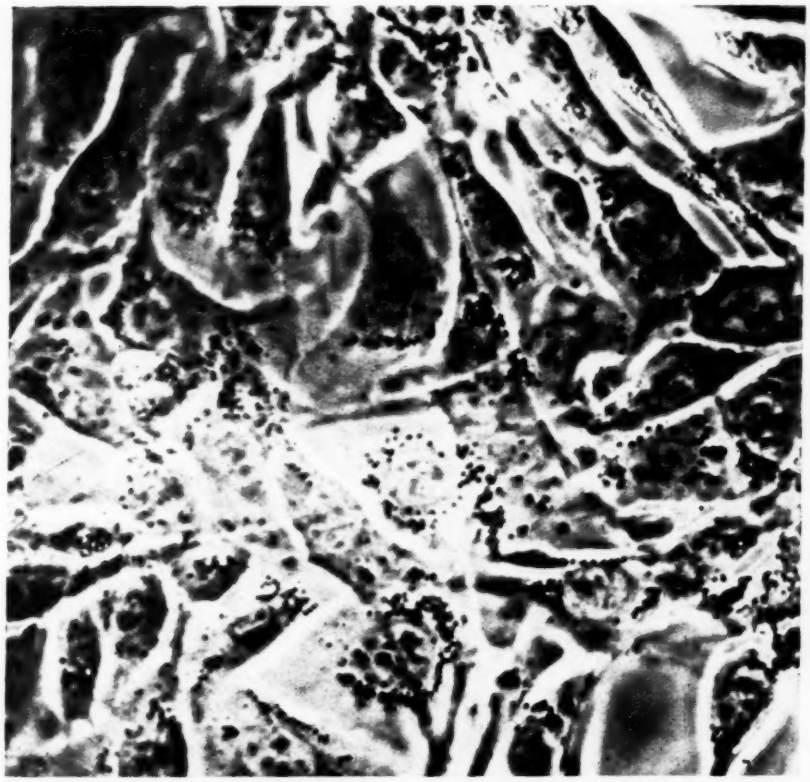


FIG. 1.—C3H sarcoma; not frozen and not desiccated. Control culture. Growth *in vitro* after 24 hours. Liquefaction. Phase-contrast photomicrograph. (× 690.)

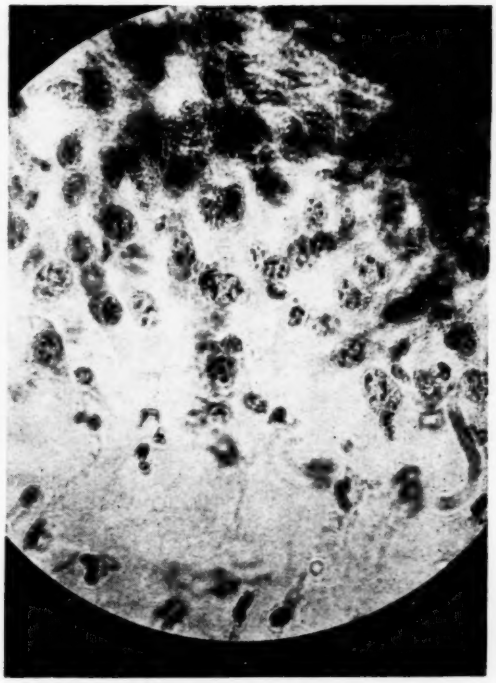


FIG. 2.—C3H sarcoma; not frozen and not desiccated. Control culture. Growth after 24 hours. Haematoxylin. Photomicrograph. (× 350.)

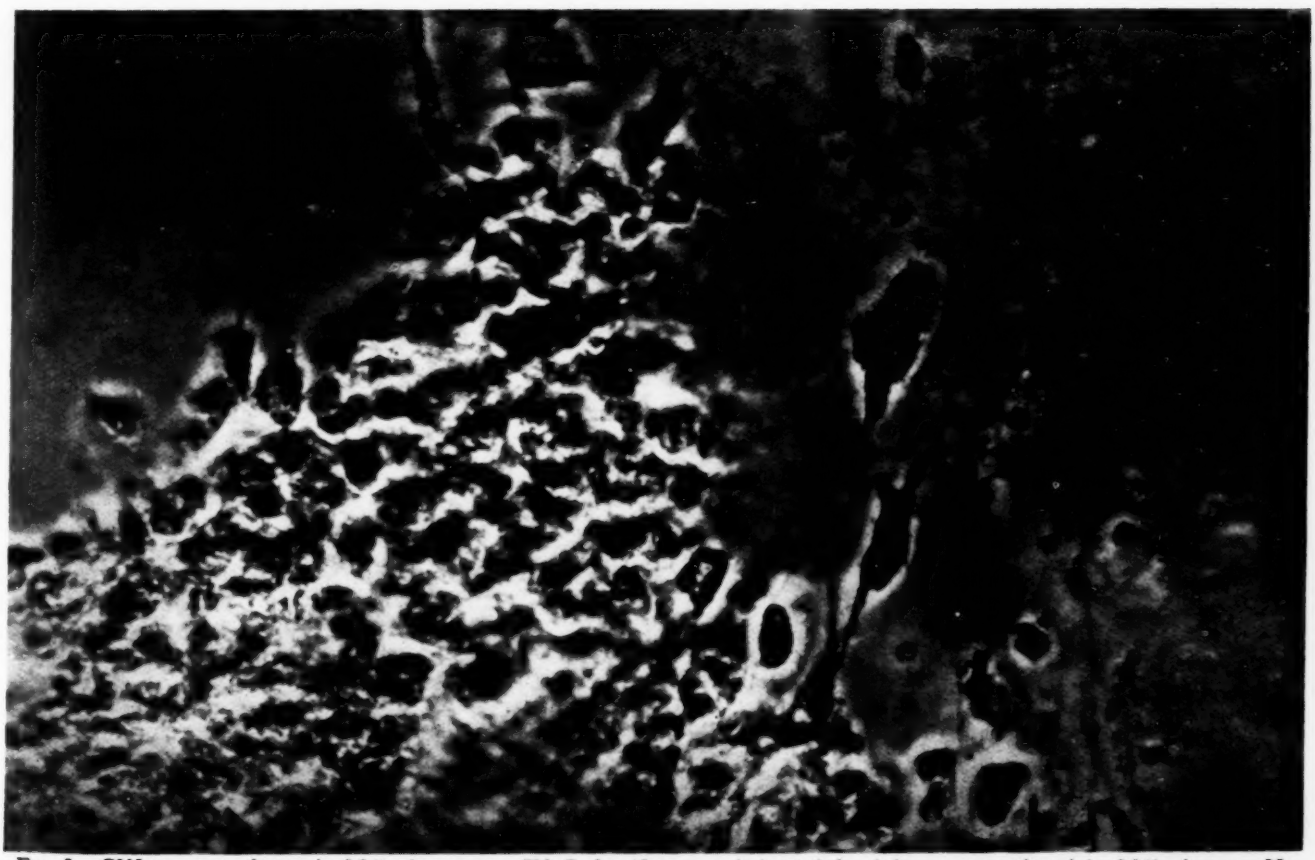


FIG. 3.—C3H sarcoma; frozen in 5.3% glucose at −79° C. for 12 hours; desiccated for 1 hour; reconstituted in 5.3% glucose. No growth *in vitro* after 24 hours. Phase-contrast photomicrograph. (× 690.)

FIG. 4.—C3H sarcoma; frozen in 5.3% glucose at −79° C. for 12 hours; desiccated for 1 hour; reconstituted in 5.3% glucose. Growth *in vitro* after 24 hours. Phase-contrast photomicrograph. (× 690.)

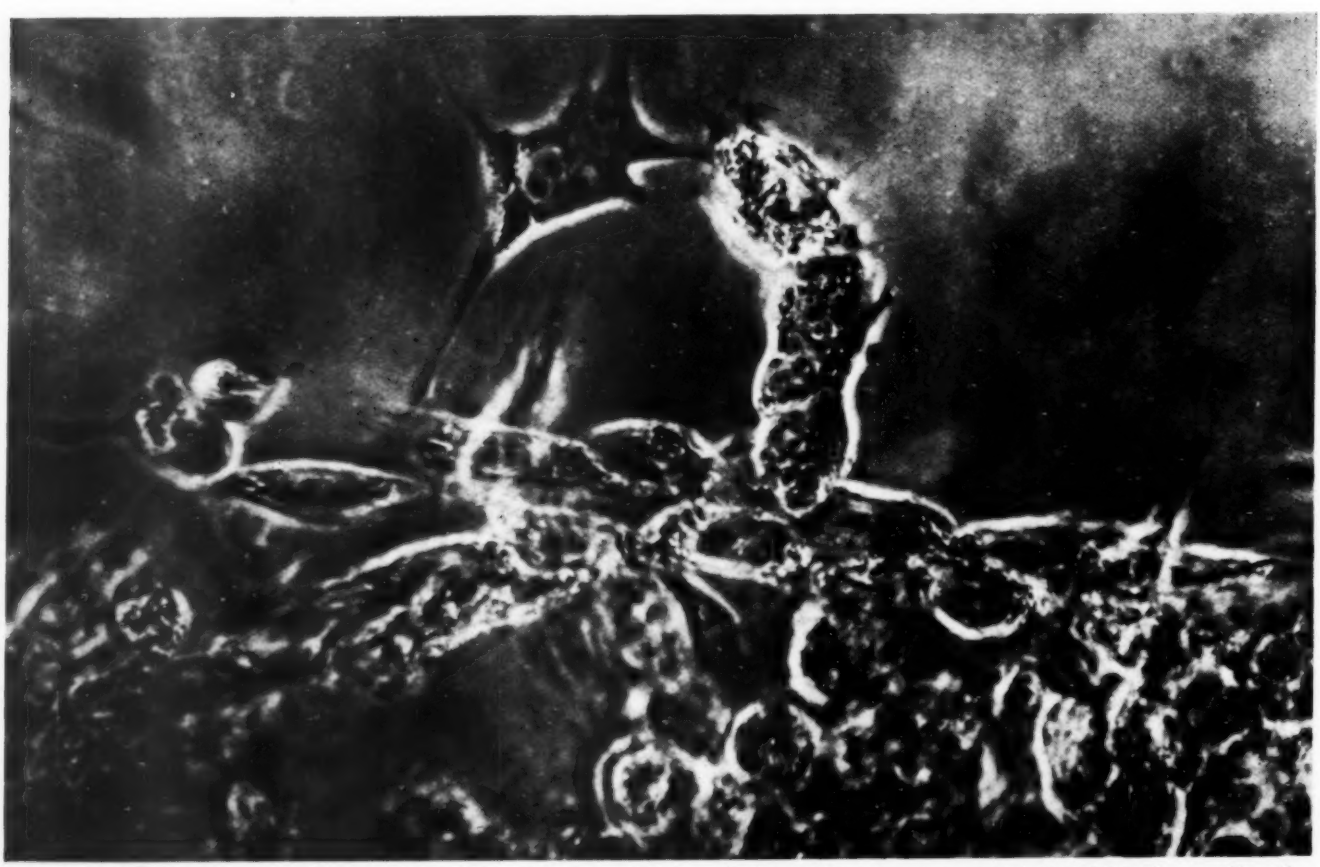


FIG. 5.—C3H sarcoma; frozen in 5.3% glucose at −79° C. for 12 hours; desiccated for 1 hour; reconstituted in 5.3% glucose. Growth *in vitro* after 24 hours. Phase-contrast photomicrograph. (× 690.)

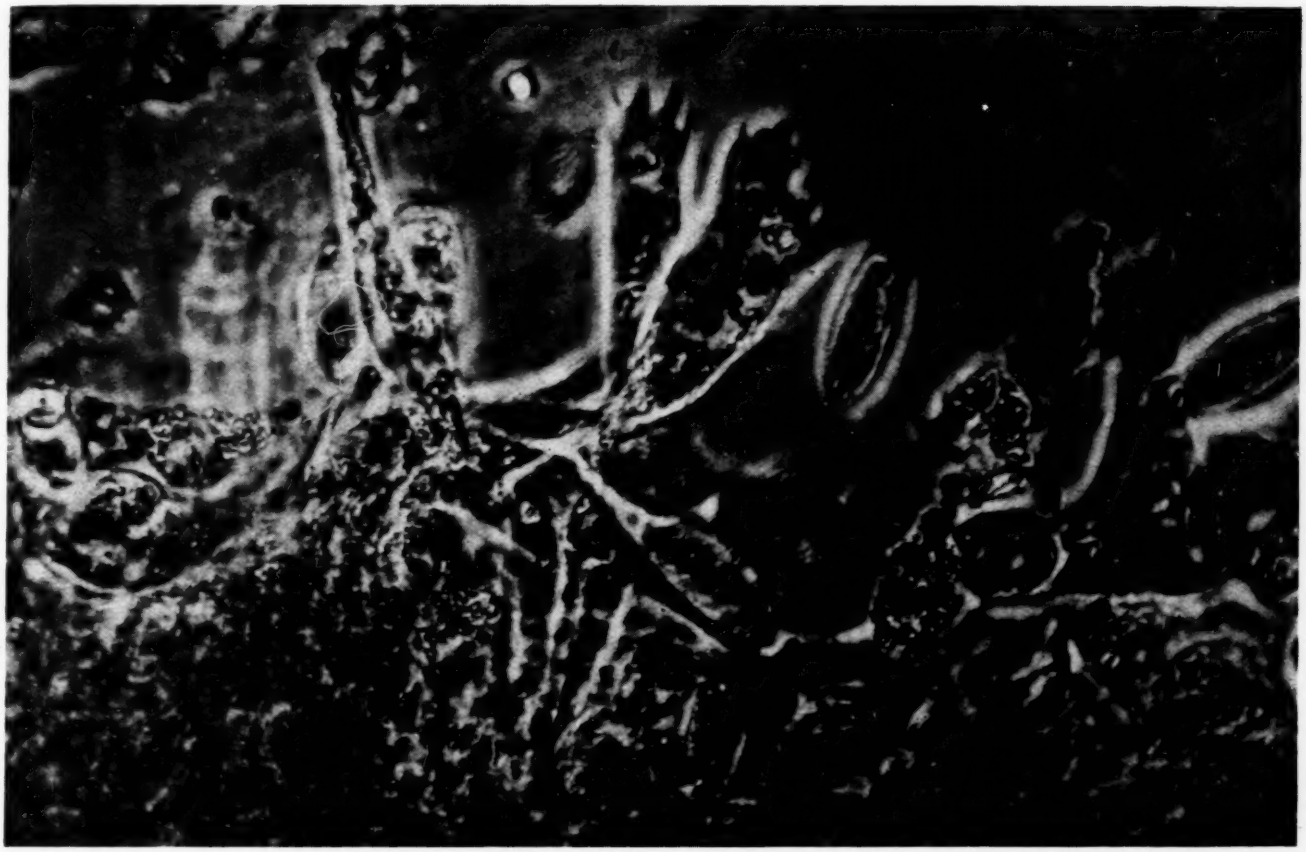


FIG. 6.—C3H sarcoma; frozen in 5.3% glucose at −79° C. for 12 hours; desiccated for 1 hour; reconstituted in 5.3% glucose. Growth *in vitro* after 48 hours. Phase-contrast photomicrograph. (× 690.)

FIG. 7.—C3H sarcoma; frozen in 5.3% glucose at −79° C. for 12 hours; desiccated for 1 hour; reconstituted in 5.3% glucose. Growth *in vitro* after 48 hours. Phase-contrast photomicrograph. (× 690.)

FIG. 8.—C3H sarcoma; frozen in 5.3% glucose at −79° C. for 12 hours; desiccated for 1 hour; reconstituted in 5.3% glucose. Growth *in vitro* after 48 hours. Phase-contrast photomicrograph. (× 690.)

FIG. 9.—C3H sarcoma, frozen in 20% glucose at −79° C. for 12 hours; desiccated for 1¼ hours; reconstituted in 20% glucose. Growth *in vitro* after 48 hours. Haematoxylin. Photomicrograph. (× 330.)

FIG. 10.—C3H sarcoma; frozen in 20% glucose at −79° C. for 12 hours; desiccated for 1¼ hours; reconstituted in 20% glucose. Growth *in vitro* after 48 hours. Phase-contrast photomicrograph. (× 690.)

FIG. 12.—C3H sarcoma; frozen in 20% glucose at −79° C. for 12 hours; desiccated for 30 minutes; reconstituted in 20% glucose. Growth *in vitro* after 48 hours. Phase-contrast photomicrograph. (× 690.)

FIG. 11.—C3H sarcoma; frozen in 20% glucose at −79° C. for 12 hours; desiccated for 30 minutes; reconstituted in 20% glucose. Growth *in vitro* after 48 hours. Growing edge of culture. Haematoxylin. Photomicrograph. (× 330.)

FIG. 13.—C3H sarcoma; frozen in 20% glucose at −79° C. for 12 hours; desiccated for 30 minutes; reconstituted in 20% glucose. Growth *in vitro* after 48 hours. Growing edge of culture with cell division. Haematoxylin. Photomicrograph. (× 700.)

FIG. 14.—C3H sarcoma; frozen in 20% glucose at −79° C. for 12 hours; desiccated for 1½ hours; reconstituted in 20% glucose. Growth *in vitro* after 48 hours. Growing edge of culture with cell division. Haematoxylin. Photomicrograph. (× 700.)

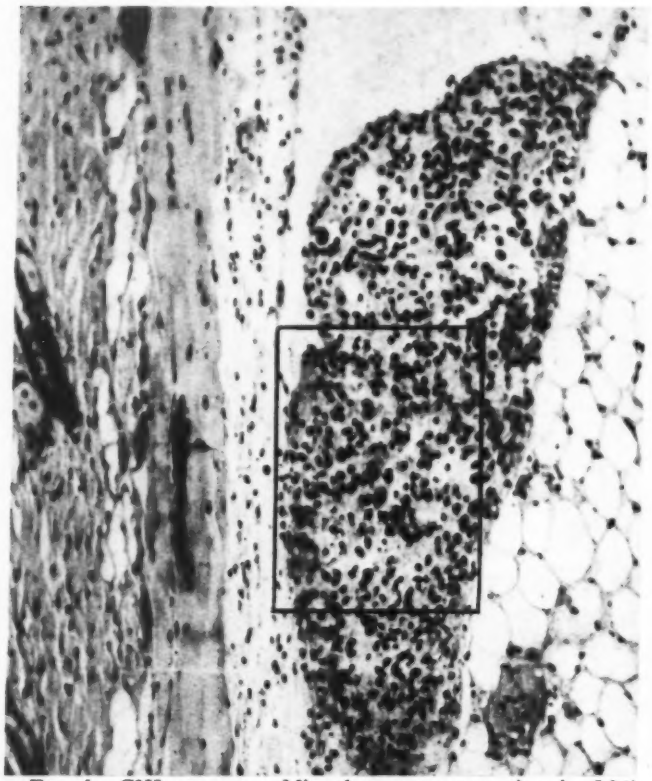


FIG. 1.—C3H sarcoma. Minced tumour suspension in 5.3% glucose; frozen at −79° C. for 12 hours; desiccated for ½ hour; reconstituted in 5.3% glucose; clotted in rat and fowl plasma and chick embryo extract. Appearance of clot *6 hours* after grafting into mouse. H. and E. (Low power, approx. × 150.)

FIG. 4.—C3H sarcoma. Minced tumour suspension in 5.3% glucose; frozen at −79° C. for 12 hours; desiccated for 1 hour; reconstituted in 5.3% glucose; clotted in rat and fowl plasma and chick embryo extract. Appearance of clot *5 days* after grafting into mouse. H. and E. (× 1,100.)

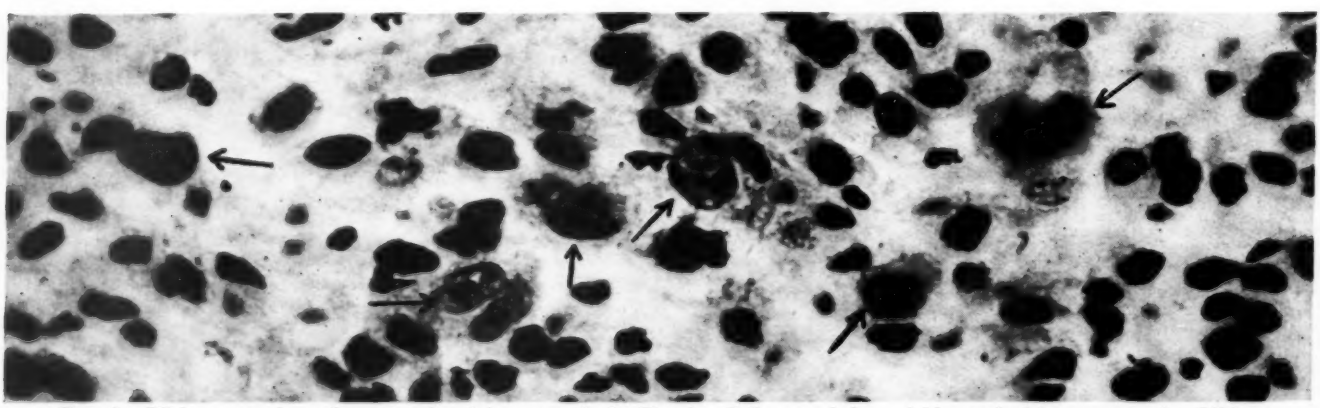


FIG. 2.—High-power view of area enclosed in rectangle in Fig. 1. Cells regarded as viable marked by arrows. (× 740.)

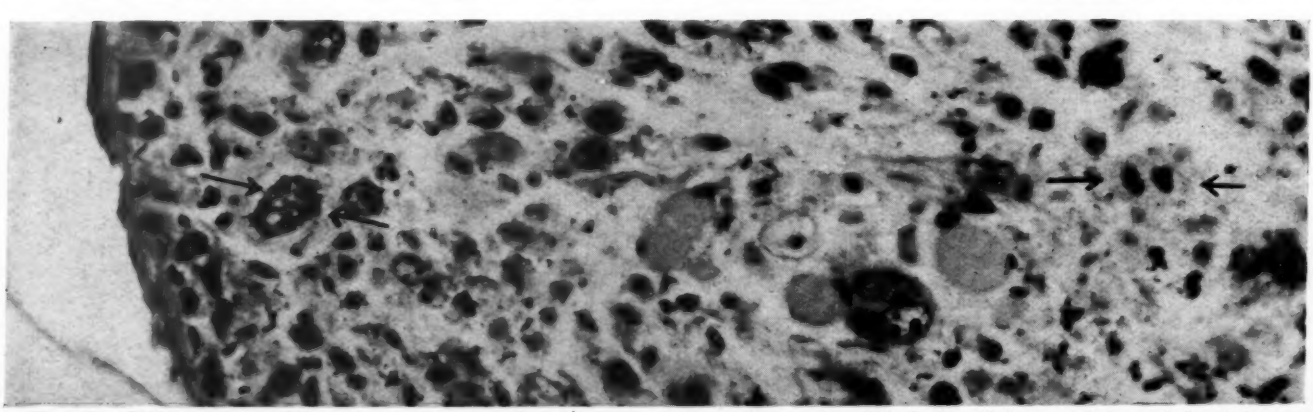


FIG. 3.—C3H sarcoma. Minced tumour suspension in 5.3% glucose; frozen at −79° C. for 12 hours; desiccated for ½ hour; reconstituted in 5.3% glucose; clotted in rat and fowl plasma and chick embryo extract. Appearance of clot *18 hours* after grafting into mouse. Mitoses seen. Cells in mitosis marked by arrows. H. and E. (× 650.)

risk. Following upon the decision to supply spray-painting equipment to all ships, the Admiralty set up a committee to draw up regulations for the protection of the operator, and this committee had nearly completed its report. A point not always appreciated was that spray painting entailed explosion and fire hazard.

Arising out of another inquiry in the dockyards a committee had been appointed with representatives of the three Services and other Government departments to select the most suitable type of respirator for processes giving rise to toxic vapours or dusts. It was well to remember, however, that in such circumstances respirators were really the second line of defence, the first line being such measures as exhaust ventilation, enclosure of operation, or other means to reduce the concentration of vapour or dust to which the workman was exposed.

Mr. Frederick also mentioned the special health hazards in submarines, in particular the danger from exhaust discharge from the engines. The Royal Navy included in its personnel many divers. These men, when wearing the conventional diving-suit, were liable to compressed-air illness if the descent was too rapid or to nitrogen narcosis if working at great depth. Even at shallow depth with their self-contained equipment they might suffer from severe oxygen poisoning.

Industrial Health in the Army

Colonel M. R. BURKE said that many of the industrial hazards which might be encountered in the Army were similar to those met with in civil life, but there were some hazards peculiar to the Service. Most of the ordinary industrial hazards concerned were met with at base installations, such as bakeries, petrol, oil, and lubricant installations, laundries, and workshops of various sorts, but they were also encountered in operational units. Many of the skilled trades in civil industry had their counterpart in the Army, but there were some occupations peculiar to the Service, such as work on searchlights. A large number of civilians were actually employed in the Army, particularly in base installations.

The Army health organization as a whole extended from the War Office, with ramifications at home and overseas so as to cover the whole Army, even down to the smallest unit, but in peacetime, owing to shortage of personnel, the coverage was not nearly as extensive as in war. It might not be generally appreciated that the provisions of the Factories Act and of the various orders and regulations made thereunder applied to the Army in the United Kingdom, subject to certain exemptions which might be authorized by the Secretary of State during public emergency. Army workshops (which were classified as factories under the Factories and Workshops Act) were open to inspection by factory inspectors, and the inspectors concerned were available for advice on technical matters. The situation in the commands overseas was somewhat difficult, because naturally the provisions of the Acts and the orders and regulations had no statutory force outside the jurisdiction of H.M. Government; but every effort was made to conform to them and also to any local government ordinances in force in the civil community.

Various industrial risks were made known from time to time through Army Council instructions. A fairly recent one was on beryllium poisoning. Circulars and technical memoranda were issued drawing attention to hazards and preventive measures, and these were circulated through departmental channels. Standard codes of practice were issued by the engineers in respect of electrical installations, and posters were used to encourage the proper care and maintenance of machinery.

Great importance was attached in the Army to medical examination of personnel, both military and civil. "Pulheems"* was designed to provide an assessment of the individual's capacity for work and to assist in passing men to the employment for which they were most suited. It was believed that the Pulheems classification, if properly carried out, enabled the right peg to be fitted into the right hole. Civilians employed by the Army, unless in casual employment for less than six days, had to be examined by a medical officer before starting work and to be passed fit for the employment in which they were engaged.

Colonel Burke also referred, as the first speaker had done, to the committee working on respirators: as many as 200 different kinds of respirators had been in use in the Army. Another committee had published a series of monographs on industrial health, and a handbook had been compiled which would be of use to all three Services. Every Army medical officer had to render a monthly report, including a special section on industrial health, and by this means quite a number of points had come forward for further research. Probably the commonest industrial hazard in the Army was dermatitis, usually in such forms as oil dermatitis and bakers' itch, but also as a disability among those handling certain textiles. Equipment returned from overseas had to be carefully dealt with from this point of view.

The Royal Air Force

Group Captain C. CROWLEY addressed the Section on aspects of industrial hygiene in the Royal Air Force. He said that there were industrial health problems peculiar to the specific functions of the different commands. Thus with air crews account had to be taken of such things as the effect of noise, of high altitudes, of cold, and of fatigue. Specially trained medical officers who were themselves pilots dealt with problems peculiar to aviation. In the maintenance commands, on the other hand, they were faced with the varied problems found in industry as a whole. In those commands Service and civilian employees were engaged in industrial work in units scattered throughout the country, and each unit might be regarded as a factory. Much had been done to bring the conditions in such units into line with modern industrial requirements, but in some cases almost insurmountable difficulties were encountered. He did not wish to give the impression that the conditions in Air Force workshops did not meet the requirements laid down in the Factory Acts, but those requirements referred to minimum permissible standards only. In fact he believed the hygienic and amenities provision in Air Force establishments compared favourably with those of industry generally.

The speaker then reviewed a number of industrial operations entailing special risk. The types of welding carried out were oxy-acetylene and electric. The hazards in this occupation were largely due to the effect of the short ultra-violet rays on the unprotected eye, resulting in keratitis and conjunctivitis. Shields and goggles were provided to meet this risk. Burns on the arms could occur during welding, and this danger was met by the provision of leather gloves. He also mentioned the dangers of "doping," at one time the cause of a number of cases of toxic jaundice. The danger was in the inhalation of the toxic solvent used in the manufacture of the dope. Amyl acetate fumes if inhaled would cause headache, gastric upset, dizziness, and irritation of the eyes, and butyl acetate caused similar symptoms. He described the means of preventing the worker from inhaling the fumes, and discussed other precautions against recognized dangers.

After studying the medical services in Korea and the Far East Command, Major-General Raymond W. Bliss, Surgeon-General of the U.S. Department of the Army, stated that a truly remarkable record was being accomplished in the protection of health and saving of life by members of the military medical services in the Far East. In the second world war, he said, three out of every four wounded men admitted to hospital were returned to duty. Outstanding as this record had been, present indications were that it would be surpassed. Admissions to hospital for disease in Korea were only slightly higher than for wounds and non-battle injuries. The disease record there became almost spectacular, he said, when one remembered that Korea had been the point of origin of some of the most extensive epidemics the world had ever known, including those of cholera, plague, dysentery, typhus, and typhoid fever. Although the soldiers frequently were forced to spend long hours, even days, in rice paddies fertilized with human excreta where the water was highly contaminated, the number of cases of dysentery had been held at a minimum.

*See *British Medical Journal*, 1949, **1**, 83.

Correspondence

Distinction Awards for Charity

SIR,—I should like to add my support to Dr. E. C. Warner's excellent letter (November 4, p. 1060). Lord Moran is certainly mistaken in thinking that the number of uneasy agnostics among consultants is inconsiderable. The idea of "distinction awards" caused great uneasiness from the outset, though, as a profession, we were perhaps not active enough in our opposition to the suggestion.

Nevertheless, many committees as well as many individuals, as a protest against the system, refused to help in the invidious task of grading their colleagues. They presumably took this course because they felt that the principle of secret awards was wrong, and surely a principle, once it has been accepted, should stand above financial considerations.

The hospital consultants have nevertheless been graded, whether they wished it or not, into classes A, B, C, or Nil. Many individuals do not wish to profit by a system for which they have shown their dislike by refusing to assist in recommendations to the grading committees. Some of them have merely refused the awards; to others the suggestion of transferring the money to a benevolent fund appeals as being more practical. An annotation in the *Journal* (November 11, p. 1106) shows how welcome contributions to these funds would be.

It is surprising and most undesirable that secret awards of this kind can be made from public funds. In the eyes of many of us they confer no distinction on the recipient.

Those who feel that this system of awards is another step in the direction of consultants becoming full-time servants of the Ministry of Health rightly remember the old tag: *Timeo Danaos et dona ferentes.*—I am, etc.,

London, W.C.1. KATHARINE LLOYD-WILLIAMS.

Employment of Epileptics

SIR,—In his interesting and useful article, "Management of the Epileptic" (November 4, p. 1047), Sir Charles Symonds discusses briefly the choice of occupation for these unfortunate people. He says that "occupations or professions for which a medical examination is required are generally barred." This statement needs amplifying. Some occupations—for example, transport driving, work with moving machinery, building and constructional work, or active service with the armed Forces—are obviously unsuitable, but the epileptic whose fits can be controlled by drugs or only occur at night and whose mental capacity is adequate can undertake a wide variety of jobs. Lennox and Cobb in 1942 in a survey of 1,000 epileptics found that 25% were unfit for ordinary employment, while 30% showed some degree of mental retardation or deterioration. Experience in placing epileptics who are registered disabled persons suggests that about half are unfit for open employment, and there is no doubt that frequent major fits occurring without warning render the individual able to work only under sheltered conditions—for instance, in a Remploy factory.

Nevertheless, many epileptics can and do work in industry and the professions on equal terms with others, and where pre-employment examinations are required these people are helped rather than hindered in obtaining suitable work. Unfortunately the epileptic, like the person with tuberculosis, conceals his disability and thereafter lives in dread of dismissal if he should have a fit while at work. Employers are loath to engage epileptics because, apart from the danger, even the most minor seizure causes disturbances in the workshop. Both management and men need to be told how to deal with the worker who has a fit, and here the doctor can be of great service.

The aim of pre-placement examinations is to fit people into suitable work, *not* to turn them away on account of some physical or mental disability. It would seem, therefore, that, far from being a bar to employment, such examinations are eminently desirable in the case of epileptics, who require even more care in placement than the majority of disabled persons.—I am, etc.,

Edinburgh. CATHERINE N. SWANSTON.

Special Centres for Child Health

SIR,—The interest and importance of Professor Alan Moncrieff's address (October 7, p. 795) may be measured by your own editorial comment and by the correspondence that has followed. The subject he covers with such practical grasp, knowledge, and wisdom is more than a field of medicine, it is a continent of changing life. How difficult and troublesome are the problems he raises; but how important, and touching the core of national health and well-being.

He urges that in the future there must be changes in the infant-welfare and school medical services to meet the changing emphasis and needs of their clinical work; and, giving examples of the present defects, he suggests remedies. To his list I add another, which has been partly tried and seems worthy of discussion. This is that the chain of infant-welfare and school medical clinics of the larger local authorities should include a principal clinic of special composition and functions. This special clinic based on a maternity hospital, which the babies (or a proportion of them) born in that hospital would continue to attend after discharge and throughout infancy and childhood, would give plenty of clinical material for the following purposes: routine continuous supervision and care of infants and children; the study of normal physical and mental development and their underlying physiological and psychological processes; the study and treatment of the great mass of minor and chronic disorders at this time of life; a training school for their own staffs (health visitors and medical men and women), social workers, and medical students; and a consultative clinic for the other clinics of the chain. The leaders and staff (nursing and medical) in this central clinic would be experts in the special field of social medicine, and would require no assistance in this special field from hospital paediatricians; and from such clinics manned by specialists in child-welfare there might be expected a flow of published studies that would advance knowledge in this field. The rest of the clinics (infant-welfare and school medical) would be largely in the hands of expert health visitors, with a medical check or ready access to the special clinic for consultation.

The provision in many areas of facilities for the deep study of this great range of preventive problems in child medicine, and the interest of their clinical application, would powerfully attract young medical men and women of talent. Such clinics would refresh and stimulate the interests of their nurses and doctors, would raise more rapidly the standard of child health, and would maintain and increase the prestige of the local authorities. So at least it appears to my enthusiastic mind; and also to fill in the meaning of Professor Moncrieff's own enthusiastic phrase about "the magnificent opportunity" that awaits a reorganization of these services. Without the attraction of work and study of this kind, I do not believe that our ablest men and women will look at a career in the infant-welfare and school medical services in their present structure and activities.—I am, etc.,

East Lothian, Scotland. CHARLES MCNEIL.

Useless Routine Medical Examinations

SIR,—Dr. Thomas Gibson's remarks (October 28, p. 1001) on useless medical examinations in children are no less applicable to adults. The main defect is that those who demand them rarely have any clear idea of what they are looking for and why. There are, of course, notable exceptions such as life offices and armed Services. When a pointless medical is demanded by an organization it becomes misleading as well as costly, because its results are used by those who are not qualified to interpret it. I recall the anxiety of a gardener summarily dismissed from county council employment because he had mild hypertension. That was the "regulation." Many firms now pay for "a medical" without any object in view other than a vague urge to do the right thing and be up-to-date. It seems churlish to greet this good will with intransigent questions of what they want: is it to be assured that the candidate will live

long enough to pay for his widow's pension, or die soon enough to save retirement annuity, or be healthy enough to need no sick pay ?

The worst sinners are the Ministries, because their mistakes are magnified a thousandfold. All hospital employees under the N.H.S. must go through the initiation ceremony of a medical examination. At first each had to be certified as being "free from any physical defect or disease which now impairs his capacity satisfactorily to undertake the duties of the post for which he is a candidate, or appears likely to prevent continuous effective service in the future." The last clause was soon deleted, possibly because examinations revealed that some would fall sick and all would die. It is difficult to see any point in the certificate as it now remains, or what a medical examination has to do with it.

Our masters are now concerned with the cost of it all, and we may be permitted to concern ourselves too. Clearly no medical examination should be called for unless the originator can answer two questions: (1) What are you looking for ? (2) What difference will it make anyway ?—I am, etc.,

London, W.1. J. B. HARMAN.

SIR,—As an A.C.M.O. of fairly recent appointment, I should like to add my views in favour of the routine school medical inspection. On completing two and a half years of various junior house appointments, including nine months at a children's hospital, I was left with an impression that the dullest of all occupations would be that of school M.O. Four years of this and infant-welfare work have proved my error. I can understand anyone who has never done routine medical inspections thinking them a waste of time, but those who have and who still look upon them as time wasted should not be doing public health work.

Unlike the interest and drama involved in hospital work, where the diagnosis can be proved by pathological and mechanical means if necessary, at routine medical inspections one has to base one's reasons for suspecting ill-health on experience gained from observing large masses of healthy children in the nude, and from having the time to listen to the sometimes meandering talk of parents. At the same time one has the opportunity of following up the child at the local school clinic, and also after working in the same area for several years of getting to know the families. Few general practitioners have time for this under existing circumstances, so why try to prevent the school medical officer from acquiring the experience ? If he waits at the school clinic for children to be sent at the discretion of others, he will just be confronted with the otorrhoeas and mouth-breathers and puny children for whom he will have no basis for comparison, and many children in borderline health will be missed, together with the loss of opportunity of advising parents.

I think that the greatest defect in the child-welfare service is not the time spent in routine medical inspections, but the complete lack of contact between the general practitioner and the public health medical officer, which seems to breed a feeling of distrust between them. As the practitioner himself cannot carry out also the functions that are fulfilled by the school and infant-welfare officer, then I suggest that arrangements should be made whereby they could meet periodically and inform each other of the few children who need special attention and discuss points of treatment. One is often handicapped at a clinic by knowing that a child would benefit from some form of treatment, and yet one cannot ensure that it is carried out, as the general practitioner may have different views. A private chat would help a lot in mutual understanding.

I should also like to add, in reply to Dr. T. Gibson (October 28, p. 1001), that I find the new medical cards, if used with common sense, very time-saving so far as the actual medical section goes, and for a healthy child can be completed in about 30 seconds. As for the graph cards, we have not got them in our area, and the heights and weights are recorded in figures. I do agree, however, that wholesale weighing and measuring is a waste of time and should be restricted to special cases.—I am, etc.,

Gatley, Cheshire. AITOLIA ENGLISH.

SIR,—As a school medical officer of many years' experience who now devotes his time in this work almost exclusively to boys in the secondary and grammar schools, I should like to voice my complete disagreement with the views expressed by Professor Alan Moncrieff (October 7, p. 795) and Dr. T. Gibson (October 28, p. 1001). Only too often these examinations are conducted by a bored staff who either are not given sufficient time to take any interest in the job or entirely fail to comprehend that there can be intense interest in the variations of the human form when seen in large numbers. Of course the mere recording of heights and weights is a waste of time, like everything else connected with the work, if no use is to be made of the data, but I would ask those in authority to allow their school medical officers more time, which they can utilize for interesting research, to allow them to think not only in terms of tonsils, hearts, and lungs, but to broaden the scope of these routine examinations.

In my inspections tests for colour blindness, inspections of ear drums by electric auroscope, examinations for undescended testicles and hernia, together with an intelligent use of the age, height, and weight data by the over-despised Tuxford index, are done in every boy examined, and the results, as judged by the interest of the boys themselves and their parents, have definitely shown that the extra time taken is well worth while. When I inform a parent that his 15-year-old boy still has both testicles undescended and suggest that further advice be sought ; when a partially colour-blind boy comes to me and asks whether it is any use his swotting for an examination for the Services or should he give up the idea ; when a young boy as a result of my talking to all in his class finds he is not the only one who thought ghosts were following him up the stairs at night and now goes up to bed alone without fear ; or when I ask the parents to let me know if their boy shows any apparent falling off in his usual robust health, since his Tuxford index at 15 is greatly below what it was on entry to the school, for which I can find no cause, and all the other boys in his form show a big increase in this index figure (these are all actual instances and could be multiplied many times over)—can it be said that I am wasting my time ? I think not.

The real value does most emphatically lie in the routine examination and the re-examination of all the children, but this must not be scamped, and there is a real need for encouragement to be given to school medical officers to look upon the value of the excellent opportunities they have in the mass of their material, to take up some particular feature, to know their children, and to make sure themselves that they are doing a job of really useful work.—I am, etc.,

Brecon, Wales. W. F. W. BETENSON.

SIR,—Dr. Cecilia Galton (October 28, p. 1001) has stressed the value of routine school medical inspections as a means of health education. Surely she is right. How often in general practice is one called in to an illness largely caused by years of neglect of the rules of health ; especially, I would say, by faulty diet. How often has one said to oneself: "If only I, or another doctor, had been there at the beginning." The school doctor *is* there at the beginning and can advise the mother, who as Dr. Galton says might hesitate to harass a busy practitioner until the child is really ill. Especially I think does this apply to children from not-so-good homes, whose mothers do not realize the child's subnormal health or the reasons for it, and who are in great need of help. The medical inspection is of course followed up by visits from the school nurse, for friendly supervision and continued education in the matters of diet and hygiene.

Surely the school doctor is part of a team: midwife, health visitor, clinic doctor, school doctor, school nurse, general practitioner, specialist, all have their part to play, and each part is important. Each player in the team must of course be continually conscious of his fellow players and of his particular job in the team. For instance, in the case of the school doctor it is essential that he be in friendly contact with the child's general practitioner, and that the mother should know this is so. In cases needing the family doctor's attention it is well to say: "Go and have a talk with Doctor," and send a letter to the doctor, saying: "I am sending Tommy Jones to see you.

What do you think about his heart, or chest, or stomach ? "—leaving the treatment where it should be, in the hands of the family doctor, but ensuring that he sees the cases that would otherwise not go to him, and strengthening his hands by continued advice to the mother about the primary laws of health and the needs of the child's body.—I am, etc.,

Kendal, Westmorland. FRANCES M. TAYLOR.

The Position Assumed by a Dead Body in Water

SIR,—I have lived most of my life on the banks of the Thames, and my many riverside friends, boat-builders, lock-keepers, and the like, all tell me that a woman after death floats face downwards, but a man floats on his back. I confirmed this statement when I was working in the Mortlake mortuary by visiting the Thames River Police, who had a station quite close. I made friends with the congenial Yorkshire coxswain of the police launch, who assured me that women invariably floated face downwards, and he added, " If ye see a roomp sticking oop, sirr, ye may know well it's a 'ooman. . . . "

I have recently been delighted to find that John Speed (1552–1629) says quite a lot about this in that entertaining but sadly neglected work *The History of Great Britaine*, first published in 1611, and his explanation is intriguing. He tells us that the women-folk of the ancient Britons at one time painted and tattooed their bodies, but gradually as they became more modest they began to clothe themselves lest " they expose to view that which nature most endeavoured to hide as knowing it least worth the viewing," and he goes on to say that it has been observed " that women being drowned naturally swimme with their face and foreparts downwards whereas men doe contrary, as if the impression of modesty were not to leave a woman even after death."

These observations were made by one, Cornelius Agrippa, in his book *De Laude Feminarum*, which he dedicated to Margaret, Duchess of Burgundy, who unfortunately was so impressed by his observations on modesty that she elected to die when she broke her thigh in a fall from her horse, rather than expose it to the gaze of her chirurgeon. Agrippa (1486–1535) was a physician, occult philosopher, and magician in the service of the Emperor Maximilian I. He is well known to all of us as " The Tall Agrippa " of *Struwwelpeter*, who punished the naughty little boys for teasing a blackamoor by dipping them in his inkpot.—I am, etc.,

Weybridge. ERIC GARDNER.

Mongolism in One of Twins

SIR,—Dr. Robert Dawson reported a case of mongolism in one of twins in a letter in your issue of August 19 (p. 461). Subsequently Dr. Dawson kindly sent me blood samples from all the members of the family. The twins have different rhesus groups as shown below:

Father	cde/cde (rr)
Mother	CDe/cde (R_1r)
Brother	CDe/cde (R_1r)
Mongol	cde/cde (rr)
Mongol's twin	CDe/cde (R_1r)

These results prove conclusively that the twins are not identical.—I am, etc.,

London, W.C.1. SYLVIA D. LAWLER.

Diagnosis and Treatment of Placenta Praevia

SIR,—In the excellent and instructive discussion on placenta praevia, reported in the *Journal* of November 4 (p. 1055), stress was laid on the great importance of modern *x*-ray methods in diagnosis. Professor F. J. Browne said that to explain the good results which had been reported the greater use of transfusion, penicillin, and the sulphonamides, together with caesarean section, must be remembered. While I agree that *x* rays should be used when possible and when occasion demands, students must still be taught that clinical observation is above everything else. Many students who are studying obstetrics will not have the chance to use *x* rays, and in domiciliary midwifery both in this country and abroad diagnosis will and must be made from the symptoms and signs.

In the last report of my mastership at the Rotunda Hospital, 1932–3, I said that with proper treatment there should be no mortality. During six of my seven years there was no mortality in 118 cases; in 1930–1 there were two deaths, one of which was caused by rupture of the uterus following the injection of pituitary extract after version by an energetic young assistant: this was an avoidable death. In other words, there were two deaths in 138 cases, many of these being *in extremis* on admission. We had to rely entirely on clinical methods of diagnosis; transfusion was never used before the birth, penicillin and the sulphonamides were unknown, and caesarean section was practised only eight times. Submammary saline was our sheet anchor. I am stating these facts to show that excellent results for the mother were obtained without modern methods. In my opinion, caesarean section should nearly always be done nowadays, in the interests of the child.

To sum up, modern methods of diagnosis and treatment must be used, but the clinical approach should be the predominant factor.—I am, etc.,

Dublin. BETHEL SOLOMONS.

Treatment of Occipito-posterior Presentations

SIR,—H. R. MacLennan states (October 7, p. 800): " Buist's pads have been advocated, and recently by no less an authority than Farquhar Murray, but we in Glasgow have been unsuccessful with this treatment." Buist was one of my teachers at the Maternity in Dundee and I cannot remember him ever demonstrating his method. I did not know that he advocated two pads. I have practised and advised the use of one pad—the size of a rolled-up serviette—placed vertically in the sulcus between the uterus and the loin muscles on the right side outside the child's back. This is retained in position by a binder, and the patient stays in bed for 24 hours and keeps her bladder empty. I use this technique not earlier than the 36th week, when the baby's head is usually either above the brim or just dipping into it. In two cases so treated one Sunday morning the baby's head was deeply engaged as an L.O.A. on the Monday morning. I consider that the two pads as used by my Glasgow colleagues must be mutually neutralizing, and hence their disappointing results as recorded. —I am, etc.,

Newcastle-upon-Tyne. FARQUHAR MURRAY.

2,665 Cases of Abortion

SIR,—May I be permitted briefly to reply to some of the questions raised on my article in the *Journal* of July 15 (p. 123) ? Professor A. M. Claye (September 9, p. 627) finds himself " incapable of believing that of 2,665 patients only 13 had a retroverted uterus." The figure is, however, correct for this series, though it includes only those cases where the retroversion was considered the cause of the abortion. It is true that retroversion is present in probably 10% of all parous women, but as a cause of abortion it is comparatively rare, a fact well demonstrated in these figures. He also apparently objects to my manipulation of the pregnant retroverted uterus into anteversion, saying that this is the simplest way to make the patient miscarry. I would point out that this procedure was only used when the retroversion was regarded as the cause of the threatened abortion, and then naturally with the greatest gentleness. It is true that the majority of simple retroversions correct themselves spontaneously during pregnancy, but in my view those referred to above definitely call for replacement, albeit with the provisos stated, though, as the figures show, the ultimate success rate is low. Professor Claye does not think my conclusion that " there is a definite though necessarily limited indication for hysterectomy in post-abortal peritonitis " is justified by the evidence given. He misread this conclusion as being arrived at on the basis of one successful case, but the basis was the comparatively large series published by Falk, H. C., and Blinick, G. (*Amer. J. Obstet. Dis. Wom.*, 1947, **54**, 314). Few surgeons can have had much experience of this drastic

procedure: my point was that it was worth definite consideration in some desperate cases.

I have no quarrel with the contention of Drs. Melvin Ramsay and J. Vahrman (August 5, p. 367) that the presence of pathogenic bacteria in the uterus is not necessarily indicative of active infection. I merely described the presence of these organisms as found in the course of a search for inclusion bodies in 50 cases, and am happy to accept the conclusions of these writers, for their experience is unrivalled in this field.

Mr. Hugh McLaren (August 5, p. 367) questions the advisability of injecting "pitocin" into the uterus, on the grounds that it occasionally causes circulatory collapse. I have seen this alarming complication on several occasions, but always in older women, and when the preparation used contained "pitressin." My feeling is that pure pitocin may safely be used in younger women whose blood volume has not been grossly attenuated by excessive bleeding.

Dr. Eustace Chesser (September 9, p. 627) finds my indications for therapeutic abortion too restricted, and the number of cases so treated too small. If Dr. Chesser thinks my interpretation of the law somewhat narrow, I can only reply that I believe it to be the correct one, and his arguments do not convince me to the contrary.—I am, etc.,

London, W.1 ALBERT DAVIS.

Mercury and Pink Disease

SIR,—Professor W. S. Craig has given an interesting and vivid account of the typical signs and symptoms of pink disease (September 30, p. 773). It was inevitable, with our lack of knowledge of the aetiology and treatment, that the discussion of these aspects of the disease should have been short. The suggestion of Warkany and Hubbard that mercury might be an aetiological factor cannot, I think, be ignored without proof to the contrary. During the last fifteen months I have come across 16 cases of pink disease in various stages of development. Of these only four were "typical." The greater number presented as cases of marked irritability, anorexia, tachycardia, and hypertension. I have recorded systolic blood pressures of 160 mm. Hg in infants. Accurate analyses (by Mr. D. Gray, of the South African Council for Scientific and Industrial Research) have shown appreciable quantities of mercury in the urines of these children, ranging from 14 to over 2,000 μg./litre. In controls mercury has been found present from 0 to 80 μg./litre. In South Africa "teething powders" are frequently used. While the most popular powder contains no mercury, there are large numbers of other powders on the market with considerable quantities of calomel. Some of my controls are children who have had such teething powders but presented no symptoms of pink disease.

The most interesting result of my investigations has been the response to B.A.L. On account of its toxicity and method of administration I have restricted its use to the worst cases, those that required hospital admission. I have treated four such cases, with very encouraging results. In one the improvement was dramatic. The infant, who for two months previously had been very fretful, suffering from extreme anorexia, marked photophobia, and seriously ill, became transformed after four days' treatment with B.A.L. into a smiling infant with improved appetite able to tolerate our bright sunshine without attempting to cover her eyes. The remarkable change in this case stimulated me to follow up my cases and make some controlled observations. I hope to publish my results on the completion of my study.—I am, etc.,

Pretoria. BEN EPSTEIN.

Hookworms in the Throat

SIR,—You may find the following case of interest.

The patient, a girl of 21, gave a history of burning pain at one spot in the throat, associated with a persistent though slight cough, all of two weeks' duration. The burning sensation had become worse on the evening I was asked to see her. On examining the throat I could see far down on the posterior pharyngeal wall and a little to the left of the mid-line a small red wriggling worm. It was easily removed on a cotton-wool swab at the end of a thin stick, and on closer inspection appeared to have two heads. As it was impossible to identify by the naked eye, I placed the swab with the worm in alcohol and next morning examined it microscopically, when it was easily seen to be a male and female *Necator americanus* in the act of copulation.

The interesting features of the case are: the unusual site of attachment of the hookworm; the length of time (two weeks) that one or both worms must have remained attached to the pharynx in spite of regular meals having been taken; and the fact that two worms were found together in the aberrant situation. I might add that after the worm had been removed there was no evidence, to the naked eye, of damage to the pharyngeal mucosa.—I am, etc.,

St. Lucia, British West Indies. A. V. WELLS.

Mantoux Conversion

SIR,—During the past fifteen years routine monthly Mantoux testing with purified protein derivative of all negative reactors on the staff of the Cheshire Joint Sanatorium has provided us with many opportunities of observing Mantoux conversions. In almost all of these cases the development of a clear-cut and definite positive Mantoux reaction is the first proof that infection has taken place.

In about 10% of the conversions, representative of all clinical types, we have observed a reaction which strongly suggests that a positive will develop, but which subsides slowly with complete absence of induration. It differs markedly from the traumatic inflammatory reaction which subsides rapidly, and it is not of the Arthus-type anaphylactic reaction which might be ascribed to hypersensitization by repeated injections of tuberculoprotein. We have seen the reaction in people who have never had a previous injection of tuberculoprotein. At this stage no radiological or clinical changes are manifest, but in some cases the E.S.R. may be raised. When this reaction has been observed subsequent monthly tests give the same equivocal reaction. It has always been followed by a typical positive Mantoux reaction in eight to twelve weeks. The time elapsing between the initial infection with tubercle bacilli and the development of a positive Mantoux is generally accepted as from four to six weeks. Our observations suggest the possibility that in some cases the period may be longer, and that particular care should be exercised when interpreting Mantoux reactions prior to B.C.G. inoculation.—We are, etc.,

Market Drayton, Salop. LESLIE J. CUTBILL.
A. CLARK PENMAN.

Radiology and the Diagnosis of Miliary Tuberculosis

SIR,—The article on the early diagnosis of miliary tuberculosis (September 23, p. 702) by Drs. J. L. Emery and J. Lorber, with its extensive bibliographical references, is very revealing. So far, however, the true revelation does not appear to have been apprehended, which is the fact that really satisfactory chest radiography is still rather the exception than the rule. Dr. J. E. Bannen (October 21, p. 951) has gone part of the way in explaining the failure of radiology in early diagnosis, but even he has not mentioned the one all-important factor in the production of satisfactory chest skiagrams. We may have the whole gamut of fine-focus tubes, optimum kilovoltage and current, adequate distance, fine-detail intensifying screens, co-operative patient, etc., but we shall still produce an indifferent skiagram unless we have a suitable time factor. Without this, there is bound to be a varying degree of loss of detail due to movement. The movements due to cardiac pulsation and respiratory causes are well recognized, but what about that which is transmitted to the *x*-ray tube by people walking on a non-rigid floor, or that due to the passage of heavy transport? Vibration from these latter causes will completely offset the advantages of a fine-focus tube unless the time of exposure is extremely short.

Although 1/50 second is nearer the ideal, most apparatus now designed for chest work will permit of an exposure of 1/25 second, which will usually give satisfactory results. If any longer exposure time is used one must expect a considerable proportion of skiagrams which cannot be described as

satisfactory according to modern standards. As an example of technical excellence I would mention the extremely fine changes which often accompany pneumoconiosis due to the more inert forms of dust. The resultant markings on a really good skiagram are considerably less than 1 mm. thick and afford proof that miliary tubercle should be recognized at a very early stage.

I suppose the truth is that the supreme importance of the time factor is still not fully appreciated, especially among those whose aim appears to be the production of perfect studies in black-and-white rather than in a translucent grey, which is rich in diagnostic detail for those who have eyes to see. Like Dr. Bannen, I am disturbed by the statement, "It is clear that *x*-ray examination cannot be relied upon for the early diagnosis of miliary tuberculosis," not only because I do not believe it, but because I have an instinctive dislike of so dogmatic a statement in medical matters.—I am, etc.,

Stoke-on-Trent. C. BELLAMY.

The Naming of Drugs

SIR,—From their student days, doctors suffer from jargon till they become so hardened to it that no one has thought to protest against the extraordinary and insufferable jaw-crackers the British Pharmacopoeia Commission now expects us to memorize. These coiners of words to enrich the language do not seem to realize that their terms have to be remembered and written down accurately at the bedside, often when one is tired, always when no glossary is at hand.

Admittedly, good monosyllables such as soap, glass, and beer are mostly already in use, though the industrialist who gave us "lux" seems able to keep it up with "wisk." But no industrialist who wants his product used goes beyond two. We have nylon, bakelite, petrol, castrol—all easy to remember. The Forces soon reduced aeroplane to aircraft, radiolocation to radar; for the human mind is irritated by long words. Even the drug manufacturer, who naturally flatters the doctor's superintellect, sticks to three, and gives us "benadryl," "seconal," "pentothal."

But the Commission thinks nothing of phenylpropanolamine, and thinks it easy to pronounce tripennamine (may one say "tripe" for short?). Its principle is to combine syllables from the organic chemical names, but practising doctors usually know little organic chemistry and care less. It carefully avoids any therapeutic suggestion, though this is just what the clinician wants for easy memorizing. After all, there are precedents: antiseptic, anaesthetic, expectorant—we know what these words mean and have no difficulty with them. But by what Pelmanism can one associate hexamethonium bromide with the reduction of hypertension? Depressin would be a much better name. Apart from memory, words such as succinylsulphathiazole cannot even be written in one line on a prescription form unless a magnifying glass is used.

Far from discouraging terminal capital letters, let us have them. A, B, and C have never been bettered as names for vitamins, in spite of gallant attempts. Why not call the series of antihistamines anthist-A, anthist-B, and so on, instead of antazoline, chlorcyclizine, and diphenhydramine—words with no mental association at all, which merely tax an already overloaded memory? Must we continue to suffer?—I am, etc.,

Ashtead, Surrey. W. EDWARDS.

Indwelling Tube for Gastric Haemorrhage

SIR,—During the last three years there have appeared in the pages of the *British Medical Journal* articles on haemorrhage from gastric and duodenal ulcer by Avery Jones, Norman Tanner, Needham, Ogilvie, and others, and an editorial on the subject appeared in the issue of July 15 (p. 153). This series provides a remarkably informative account of the problem, but it makes no mention of a part of the treatment which is very useful and in some cases of vital importance. I refer to the use of an indwelling gastric tube with hourly or half-hourly aspiration. After each aspiration the tube is washed through with a little water to prevent blockage by clot. The aspirations are carried out immediately before feeding. I know that some clinicians think, or perhaps feel rather than think, that the tube may in some way disturb the bleeding point. But this is highly unlikely and easily outweighed by the advantages of the tube.

In gastric ulcers, and those duodenal ulcers which bleed back into the stomach, the appearance of bright blood provides direct and immediate evidence of the continuance of the bleeding, and the clinician planning treatment, perhaps operation, need not wait for these too-long-delayed and easily vitiated indirect signs such as the vomit of blood, melaena, and alterations in blood pressure, pulse rate, and haemoglobin value. In collaboration with the attending physician I have been able to arrange operation, in patients with haemorrhage from a large artery exposed in the floor of the ulcer, at a much earlier and more favourable stage when frequent gastric aspiration has been practised.

At operation the stomach and intestines are very often found filled with altered blood, decomposing and with a foul odour, and sometimes forming a jelly-like cast of the stomach and intestines. Absorption from this possibly contributes to uraemia. The prevention of this accumulation is highly desirable.

Distension of any part of the gastro-intestinal tract by blood or air or secretions (and this is particularly important when there is a complicating stenosis) causes a vascular congestion by compressing the small veins more than the small arteries. Such congestion encourages haemorrhage. The surgeon sees the proof of this at every laparotomy for intestinal obstruction. Aspiration tends to prevent this distension and congestion. Even when the patient is sleeping, perhaps under the influence of morphine, local treatment of the stomach can be continued by injections down the tube. Hyperacidity, gastritis, and erosions are sometimes of importance in gastric bleeding. It is my practice to give the patient an hourly dose of aluminium hydroxide.

I have had a few patients who have bled for some days in whom the commencement of gastric aspiration was followed by an improvement in the general condition and a decrease and subsequent cessation of haemorrhage.

—I am, etc.,

Sydney, N.S.W. V. J. KINSELLA.

Precordial Pulsation in Children

SIR,—Dr. Paul Wood's valuable account (September 16, p. 639) of his work on congenital heart disease is most stimulating and helpful to the medical profession. I have been particularly interested in his description of precordial pulsations which may be seen in cases of congenital heart disease. Here he states that "when the right ventricle is enlarged there is a diffuse lift in the third and fourth space between the sternum and the nipple line. This lifting outflow tract . . . is probably the best clinical evidence available of an enlarged right ventricle." In his paper, however, no mention is made of the age group to which this observation refers. For this reason the following fact may be of practical value. This "lift," which presumably involves the rib between the third and fourth intercostal space, is highly suggestive of an enlarged right ventricle in adults and in infants under the age of 1. This sign, however, is frequently found in children over the age of 1 without there being any electrocardiographical or radiological evidence of cardiac disease. Such cases are more common among children in the 2 to 7 years age group than in the older age groups.—I am, etc.,

Edinburgh. R. A. MILLER.

Squatting Position in Labour

SIR,—The following instance may prove of interest as an example of the great value of the squatting position in certain circumstances.

A woman aged 34 had lost her first child following a cerebral haemorrhage, as a result of (according to the mother) a twelve hours' second stage during which no medical aid was sought. A second child, therefore, was very much desired. The second labour proceeded normally and easily until the cervix was fully dilated; half an hour later the membranes presented at the vulva and were ruptured. The liquor contained a large amount of meconium, and it was then noticed that the foetal heart rate had dropped to 100 per minute. As the scalp was just showing, and the perineum was very lax, it appeared that a few good contractions would deliver the baby. However, the pains became gradually weaker and the head, after twenty minutes, had made no advance. An episiotomy was performed, but it proved of no assistance, as the head was just too high to extend the perineum during the contractions. The foetal

heart rate, twenty minutes after the original measurement, had fallen to 96, and meconium was still being passed. Preparations were therefore made for immediate forceps delivery. While the instruments were boiling, however, it was thought worth while to try the effect of the squatting position. The mother was assisted into this position on the bed, supporting herself on the shoulders of two assistants. To the gratification of all present the baby's head almost shot out of the vagina with the next pain, and was with difficulty restrained. An easy delivery followed. The child, after the removal of mucus from its throat, appeared quite fit.

It is reasonable to suppose that the adoption of this position in all probability saved the child's life, or at least prevented a cerebral haemorrhage. The mother stated afterwards that she noticed an immense improvement in the quality of her bearing-down efforts as soon as she had adopted this position.—I am, etc.,

Southampton. S. R. SAUNDERS.

Recurrent Obstruction of an Obturator Hernia

SIR,—I was most interested to read Mr. B. W. T. Pender's account of a case of recurrent obstruction of an obturator hernia (November 4, p. 1038), as I have recently seen a similar example of this rare condition.

A woman, aged 67, was admitted to hospital in November, 1949, with the signs and symptoms of acute intestinal obstruction. She complained of pain in the right thigh and knee. No hernia could be palpated, but there was tenderness in the right Scarpa's triangle. The abdomen was opened through a right paramedian incision and it was found that a strangulated obturator hernia was present on the right side, a loop of ileum being imprisoned in the sac. The hernia was easily reduced by gentle traction from within the abdomen. No attempt at repair was made, and the abdomen was closed after it had been noted that a sac was also present in the left obturator canal.

In September, 1950, the patient was admitted to hospital again with exactly the same condition. This time when the abdominal cavity was opened reduction could not be performed until the constriction had been enlarged from within the abdomen. In view of the history it was felt that repair must be attempted, but sufficient tissue could not be found for closure of the canal by simple suture. The right broad ligament was therefore sewn over the gap with interrupted silk sutures, and this appeared to give a firm repair. The defect on the left side, being small, was easily closed with silk sutures. Whether the repair on the right side will prevent further recurrences remains to be seen.

Having had this experience I would endorse Mr. Pender's view that repair in these cases seems to be important, especially as the mortality rate of strangulated obturator hernia is stated to be over 30% (Aird, *A Companion in Surgical Studies*, 1949). It is of interest that in both these cases reduction was easy at the first operation and difficult at the second.

I wish to thank Mr. J. H. Conyers and Mr. J. K. Willson-Pepper for permitting me to treat this case.

—I am, etc.,

York. P. R. R. CLARKE.

Lupus Erythematosus—an Auto-antibody Disease?

SIR,—In following up our work on auto-antibodies in the pathogenesis of disease (Gear, 1946) we are systematically investigating cases of illness which we suspect may have what may be called an auto-allergic basis. In this study one line of investigation is the testing of their sera for irregular agglutinins and auto-antibodies, and their red cells by the direct Coombs test for the presence of immune globulin. The results of the tests on the blood from patients suffering from a variety of conditions will form the subject of a comprehensive paper. It is the purpose of this short note to record the fact that in two cases of lupus erythematosus the direct Coombs test for sensitization of the red cells gave a positive result. One of these cases was the chronic discoid type. The other was of the acute disseminated type and ended fatally. The findings of the post-mortem examination confirmed the diagnosis.

A positive Coombs test indicates the presence of a circulating auto-antibody, thus confirming the observations of Wiener (1950) using the trypsin test for sensitization of red cells. It may well be that this auto-antibody plays an important role in the pathogenesis of lupus erythematosus and related conditions. If it does, then treatment with drugs or hormones which inhibit the antigen-antibody reaction should be beneficial. Sodium salicylate and acetyl-salicylic acid have been credited with this action. It seems also that one of the effects of the administration of cortisone and A.C.T.H. is to diminish the amount of antibody produced. It certainly is worth further study.—We are, etc.,

Johannesburg. A. ZOUTENDYK,
J. H. S. GEAR,
South African Institute for Medical Research.

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Latent Amoebic Dysentery

SIR,—The contribution by Dr. Angus Everard (October 7, p. 818) contains the comment, "It seems very improbable that this was a case of indigenous amoebic dysentery, and much more likely that it was a relapse from a previously unrecognized infection contracted abroad." I would like to support this concept, seeing that during my period of military service in India I was able to review several patients whose symptom complex simulated that of dyspepsia, gastric ulcer, chronic appendicitis, or chronic hepatitis. These conditions occur in temperate climates and are unrelated to any tropical infection.

In the early part of my tropical experience, treatment was given on similar lines to those adopted in this country for such conditions, but an increasing knowledge of diseases endemic in India caused a revision of opinion, and on careful examination these patients revealed *E. histolytica* or the cysts of this organism in the stool; showed typical entamoebic ulceration of the rectum and colon on sigmoidoscopy; and those which did not show the organism in the stool even after a preliminary course of sulphaguanidine responded to a course of treatment for amoebiasis as laid down in Dr. Everard's memorandum.

In the short space of six weeks in the autumn of 1944, 24 patients were assessed for abdominal symptoms, the final diagnosis being amoebic hepatitis. All these patients showed no *E. histolytica* or cysts in the stool at any time and no evidence of intestinal amoebiasis by sigmoidoscopic examination, yet all responded favourably to the specific treatment for amoebic infection. The findings may be tabulated as follows:

No. of cases with previous history of amoebic dysentery ..	8
" " " " " bacillary dysentery ..	3
" " no previous history of dysentery ..	13
Total	24
No. with symptoms relating to probable gastric lesion ..	7
" " " " " appendix lesion ..	4
" " " " " hepatic lesion ..	2
Total	13

It would be fair to postulate that infection had occurred during the preceding two years but had remained latent, and the insidious character of *E. histolytica* caused one to feel justified in one's diagnosis, which was confirmed by subsequent investigation and treatment. In fact, it is a matter of surprise that more cases similar to Dr. Everard's have not been reported in the literature since the termination of the war in the Far East and the return home of the Servicemen from that theatre.—I am, etc.,

Maidstone, Kent. D. L. PUGH.

Troubles of being Biped

SIR,—Dr. Marjory W. Warren states (October 21, p. 921). "Anatomically and physiologically man has been designed for an active existence in the upright and vertical position." Is this generally accepted? I doubt it. Is it not a fact that varicose veins in various parts—legs, scrotum, and lower bowel—uterine prolapse, cystocele, rectocele, enteroptoses, etc., are all the result of our ancestors in the years of very long ago being so foolish as to decide to walk on two legs instead of four?—I am, etc.,

Glenfield, Leicester. FILMER COLEMAN.

Refusal to Appear in Court

SIR,—In common with many practising solicitors I have been under the impression that it is an advantage, when acting for a man appearing before the magistrates to answer an affiliation summons, to call medical evidence of blood tests performed on the interested parties and on the infant.

During the last couple of weeks I endeavoured to secure this evidence, as I have such a case in hand. I met with a complete lack of co-operation from the medical profession and a complete refusal from each pathologist I approached, explaining that after making the requisite tests his attendance would be required in court to give evidence of his findings. I applied to various London teaching hospitals as well as to other hospitals and private laboratories.

I am writing to inquire if you can explain the reason for this reluctance to attend court to give evidence of the result of these blood tests, and, if possible, to know who in the London area is prepared to attend a trial in a magistrates' court to give the requisite assistance.—I am, etc.,

London, N.W.2. A. A. WALFORD.

Care and Management of Laboratory Animals

SIR,—In 1943 we were seeking information about the care and management of laboratory animals and were able, through the hospitality of your columns, to make contact with many scientists using laboratory animals. Thanks to this help and to that of certain expert writers we were able to issue in 1947 the *UFAW Handbook on the Care and Management of Laboratory Animals*, edited by Professor A. N. Worden, M.R.C.V.S. As some time has now elapsed since this book appeared we should be most grateful if we might again appeal to all persons interested in laboratory animals to send us suggestions for the improvement of the *Handbook* and any additional information which has come to their notice. The subjects concerning which information is required are as follows:

The training of animal technicians, animal houses and animal rooms, rabbits, guinea-pigs, rats, mice, voles, hamsters, hedgehogs, ferrets, frogs, and other amphibians, fish, anthropoids, dogs, cats, goats, poultry, canaries, pigeons, or any other species of animals used for scientific purposes. Subject matter can be conveniently forwarded to us grouped under the headings of anaesthesia, euthanasia, supply and breeding, feeding and watering, general management and hygiene, transport by sea, land, and air, animal behaviour and psychology.

All the information which reaches us will be most gratefully acknowledged.—I am, etc.,

284, Regent's Park Road, London, N.W.3. F. JEAN VINTER.

POINTS FROM LETTERS

Arteriovenous Shunts

Dr. I. H. J. BOURNE (Hornchurch, Essex) writes: The arteriovenous shunt has recently been demonstrated in the stomach by Professor Bentley, of Newcastle. . . . The shunt would seem to be the basic mechanism not only of Raynaud's disease, the Trueta kidney, and gastric disorders: one is tempted to forecast that this mechanism will be found to operate in all parts of the body. . . . In the case of the stomach, the shunting of blood away from the mucous membrane causes lowering of the vitality of the membrane and greater liability to abrasion or irritation. This shunt can be initiated via the nervous paths, or by direct injury, such as manipulation during operation. Of other as yet unexplained disease processes in the body, fibrositis may be taken as a good example. . . . If for any reason the blood supply to muscle fibres is cut off, the damage results in swelling of those fibres. This swelling would take place after an interval of time has lapsed. This point may be substantiated by quoting a recent theory concerning the aetiology of sterno-mastoid tumour in newborn infants. If the blood supply to a part of the sterno-mastoid muscle is cut off by pressure during the second stage of labour, the damaged muscle fibres are seen to swell after an interval of ten days. These muscle fibres have been killed, and are replaced in time by fibrous tissues. One can visualize lesser degrees of damage occurring in muscles affected by fibrositis. . . . In these cases the arteriovenous shunt system may be stimulated by the sympathetic nerves as a result of mental conflict.

Obituary

J. H. ANDERSON, C.M.G., C.B.E., M.D., F.R.A.C.P.

Colonel J. H. Anderson, who from 1924 onwards was physician at Ruthin Castle Clinic, died at Ruthin on November 4, aged 67 years.

John Hubback Anderson was born at Urana, New South Wales, where his father, the late Dr. J. F. Anderson, was in practice. The family moved to Tasmania, and Anderson was educated at Longford Grammar School. On leaving school he took a position in a lawyer's office at Launceston, but in 1904 he went to Ormond College, Melbourne University, to study medicine. He graduated M.B., B.S. in 1908, and proceeded M.D. two years later. After qualifying he became senior demonstrator in anatomy at Melbourne University under Professor R. J. A. Berry, and was later appointed honorary out-patients' physician at St. Vincent's Hospital, Melbourne. He went into practice at Benalla in 1914, but at the outbreak of war joined the A.I.F. After serving in Gallipoli, where he had a bad attack of dysentery, he had to be invalided back to Egypt. Later he went to France, and was gassed during the Somme offensive. He was twice mentioned in dispatches. Anderson then joined the headquarters staff in London, under General Sir Neville Howse, V.C., at Horseferry Road, where he became known to most of the young medical men from the Australian Commonwealth. For his distinguished services he was appointed C.B.E. in 1918 and C.M.G. a year later. He returned to Melbourne after the war and re-joined the anatomy school of the university. He gave the anatomy lectures in 1920, while Professor Berry was on leave, and later continued as senior demonstrator.

In 1923 Anderson returned to this country, and a year later became physician at Ruthin Castle Clinic in association with the late Sir Edmund Spriggs and Dr. S. W. Patterson. He soon made himself known as a sound clinical physician, and many old patients of the Clinic have paid tribute to his kindliness and helpfulness. In 1946 he became a member of Council of the B.M.A. as representative of South Australia, Tasmania, Victoria, and Western Australia. It interested him greatly to keep in touch with the advances of medical policy in this country and their repercussions on medicine in Australia. He was the London correspondent of the *Medical Journal of Australia*. During the second world war he served as Assistant Director-General of Medical Services in the Australian Army Staff in London.

Dr. S. W. Patterson writes: Anderson took an active part in the discussions on the N.H.S. Bill both centrally and in N. Wales. He was a very competent chairman of the Denbigh and Flint Division of the British Medical Association from 1938 to 1941, and besides being a member of Council he was also a member of the Dominions and Colonies and Dependencies Committees. His mind was always an orderly one; he found great difficulty in adjusting himself to changes of policy at Headquarters, and remained unconvinced of the usefulness of the National Health Service as at present constituted. Anderson associated himself with many local affairs in Denbighshire. He was commissioner for the Scouts, took an outstanding interest in the British Legion activities, and was for many years president of the county branch. He succeeded the late Sir Edmund Spriggs as chairman of the juvenile court in

Ruthin, and he was High Sheriff designate of Denbighshire for next year. Dr. Anderson, whose wife died in 1937, is survived by his son and daughter.

D. S. STEVENSON, M.B.E., M.B., F.R.F.P.S.

Dr. Douglas Stuart Stevenson, physician to the Western Infirmary, Glasgow, died in Glasgow on October 21. He studied medicine at Glasgow University and graduated M.B., Ch.B. in 1917. He at once entered, through the Navy, the early but rapidly developing medical branch of what later became the R.A.F. His services were recognized by awards of the M.B.E. and the Belgian Croix de Guerre. When he returned to Glasgow after the war Stevenson graduated into pure consulting medicine, like many of his generation, as a family physician. He was in fact for years the trusted physician and adviser of many families round about Glasgow, who will not fail to remember his skill, courtesy, and friendship. This initial phase made Stevenson, when he obtained his wards at the Western Infirmary, an ideal practising consultant physician. He was never greatly interested in research, but rather in the care of his patients and also in the situation, domestic or otherwise, created by their illness. Thus Stevenson was a splendid teacher of medical students intending to become general practitioners, and such men are becoming rarer every day. He was an honorary lecturer in clinical medicine of Glasgow University, and he became a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow in 1932. For a number of years he was consulting physician to the Ayr County Hospital and to the Glasgow Orthopaedic and Rheumatic Clinic. Stevenson served again during the second world war, becoming a brigadier and consulting physician to the Army in Scotland. His duties entailed much travel and fatigue, but he seemed to enjoy the responsibilities to the full. The war years told on his health, however, and not long after his demobilization he was gradually compelled to give up some of his more strenuous physical activities. Fortunately he was able to continue his hospital and consulting work to the end. He made occasional contributions to the medical journals, including a paper, "Famine Oedema in Prisoners of War," in this *Journal* in 1944. Stevenson's death is a great loss to medicine in Glasgow and the West of Scotland, where he was well known in many circles, not all connected with his profession. The sympathy of many friends and grateful patients will go out to his widow and his schoolboy son.—J. W. McN.

C. N. GROVES, C.B.E., M.D.

Dr. Charles Nixon Groves, a general practitioner in the West End of London for 50 years, died suddenly at his home on November 8.

Born in 1871, he was educated at Bradfield College School and Keble College, Oxford. He completed his medical education at the London Hospital, graduating M.B., B.Ch. in 1878 and proceeding M.D. in 1901. After holding the posts of house-physician and house-surgeon at the London Hospital—he was the last house-surgeon to Sir Frederick Treves—he became resident medical officer at the Royal National Hospital for Diseases of the Chest. Groves then entered general practice in the West End of London and quickly built up a reputation as a sound clinician. Only those who had the privilege of working with him could realize on what solid foundation the confidence of his patients was based. During the first world war Groves was civilian medical officer in charge of the Darell Hospital for Officers, and he was twice mentioned in the lists of the Secretary of State for War. In 1920 he was appointed C.B.E. In later years many of the great names in the Army and Navy were among his patients. He was a Fellow of the Harveian Society and of the Medical Society of London, having been at one time a member of the council of both bodies. He remained a busy and vigorous doctor until just before he died, setting out on his round of visits at an early hour every day. His was an example we should all be proud to follow.—H. S.

Sir AUGUSTUS DANIEL, K.B.E., M.B.

Sir Augustus Daniel, who died in London on November 7 at the age of 83, devoted his life to the study of art after taking a medical degree. He was director of the National Gallery from 1929 to 1933.

Augustus Moore Daniel was the son of Dr. E. M. Daniel, of York. He was educated at Repton and Trinity College, Cambridge, where he took the Natural Science Tripos, obtaining a first in both parts. He played association football for the university in 1888 and 1889. At Guy's Hospital, where he studied medicine after leaving Cambridge, he was a dresser to Mr. Arbuthnot Lane, as he then was. After graduating M.B., B.Ch., Daniel immediately turned to the study of art, though at the same time he took an active part in local government affairs, in which he gained useful administrative experience. In 1900 he was appointed assistant director of the British School in Rome, where his talent for organization proved of lasting value. He became a trustee of the National Gallery in 1925, and he was appointed to succeed Sir Charles Holmes as director in 1928. In 1931 Cambridge University bestowed on him the honorary degree of Litt.D., and a year later he was created K.B.E. Towards the end of the first world war Daniel used his medical knowledge to good effect as chairman of the board of management of the Scarborough Hospital.

Dr. JOHN MCCREA died on October 23 at his home in Wargrave, Berkshire, aged 78. His father was Dr. John McCrea, of Belfast, and John McCrea, jun., studied medicine at Queen's College, Belfast, graduating M.B., B.Chir. in 1900. He then went out to South Africa during the Boer War as a civil surgeon attached to the Field Force, and he was awarded the Campaign Medal with three clasps. In 1904 he joined his brother, Dr. Hugh McCrea, in practice at Wargrave, and after a year or two, when his brother moved to London, he carried on the practice single-handed until Dr. Black joined him in partnership in 1947. He was a great example to the younger generation of practitioners, and as an upholder of the ethics of the medical profession no one could have been more scrupulous. He took an active part in the affairs of the British Medical Association, and was vice-chairman of the Reading Division in 1916–17. For many years he was a member of the executive committee of the Division, which he represented at the Annual Representative Meetings held in London in 1917 and 1942. He was one of the original members of the old panel committee for Berkshire, being chairman for many years. For a period he was also chairman of the Berkshire Insurance Committee, and he served on numerous subcommittees of that body. He represented Berkshire on the Panel Conference for several years. At his death he was vice-chairman of the Berkshire Executive Council and chairman of the Berkshire Local Medical Committee. He also took an active part in local community affairs, and Wargrave will miss his wise counsel. He was a well-known freemason, being a past grand deacon of the Grand Lodge of England and a life governor of the Royal Masonic Hospital. It was surprising how McCrea had time for all his many activities while carrying on a large country practice single-handed, but his happiness lay in giving service to his fellow men. He felt the death of his wife three years ago very deeply, and, although his ready Irish wit was still there, it did not bubble over as it had done in the old days. The sympathy of his friends and colleagues goes out to his two daughters and son.

Medical Notes in Parliament

The Ravages of Tuberculosis

During the debate on the address replying to the King's Speech Mr. WILLIAM REID on November 2 said he was perturbed about the absence from the King's Speech of any references to the ravages of tuberculosis. In Scotland there were 41,000 tuberculosis cases and more than 3,500 deaths per annum. Among young women the death rate was double that in England. Dr. Horace Joules, medical superintendent of the Central Middlesex Hospital, had said at a conference in Edinburgh on October 28 that the tuberculosis rate in Glasgow was as bad as that in Madrid. Mr. Reid declared that the whole population of Glasgow should be radiographed within the next month. That was the considered opinion of one of the greatest tuberculosis authorities in the country. Glasgow had 12,000 tuberculous persons on the registers of the public health department, although it had one of the most efficient health departments in the United Kingdom. He appealed to the Secretary of State for Scotland and the Minister of Health to consider a crisis expansion of the tuberculosis services. In Glasgow alone 1,000 additional beds and 300 additional nurses were needed. He suggested that care of the aged, the chronic sick, and the infirm should be removed from the regional hospital boards and that accommodation less elaborately equipped and less expensively staffed should be provided for them. To find sufficient nurses for all needs he suggested an appeal to churches of all denominations and to British Red Cross V.A.D.s to assist in an emergency nursing service, under the supervision of qualified nurses.

Experiments on Animals

On the Motion for the Adjournment on October 31 Mr. PETER FREEMAN said medical science had apparently adopted only one method of research in regard to cancer, and that was vivisection of living animals performed under the Cruelty to Animals Act, 1876. Vivisection had led to the introduction of dangerous medical treatments and a deplorable waste of public money, while health-promoting measures had been neglected. In 1904 there had been 8,290 experiments on animals for cancer research. The figure increased almost every year, and reached 75,343 in 1949. About two-thirds were conducted without any anaesthetics. No inspection was permitted to anyone except a few officials appointed by the Home Office, all of whom he believed to be trained vivisectors. The money spent on this purpose was estimated at between £10 m. and £20 m. during the last half-century, and meanwhile deaths from cancer in Great Britain had risen from 26,721 in 1900 to 80,732 in 1949. All experiments had turned out to be blind alleys and there should be no further delay in abandoning animal experimentation and concentrating on the study of cancer as it occurred spontaneously in man and its relationship to every aspect of his daily life.

Dr. CHARLES HILL said the assertion that animal experimentation was futile was flying in the face of the facts. Mr. Freeman had not told the house that as a result of animal experimentation at least one form of cancer had been successfully studied and now was curable. He had ignored the enormous benefits to humanity in this and other fields from animal experiments, and preferred his woolly assertions to the calm and cold findings of science. Dr. Hill said he preferred to see animals used in attempts to induce cancerous growth than to have human beings used for the purpose. He hoped that the remarks which Mr. Freeman had made would receive the contemptuous fate which they deserved.

Mr. G. DE FREITAS, in replying for the Home Office, explained the working of the Act of 1876. He also pointed out that the comparative mortality index in the Registrar-General's Statistical Review, which allowed for the effect of changes in the age distribution of the population, showed that from year to year over the last thirty years the death rate from cancer had remained fairly constant, and each year there had been a slight reduction in the mortality of women.

On November 1 Mr. PETER FREEMAN presented a petition against the practice of experimenting on living animals. He said the petition represented that such experiments were continually being extended, and prayed that their practice should be prohibited by law. The petition was ordered to lie on the table.

Name and Identity of Hospitals

Dr. CHARLES HILL asked on November 9 whether Mr. Bevan knew that in some areas, particularly recently, hospital management committees had over-emphasized their own names on notice boards, notepaper, and the like at the expense of the hospital's local name, which had meant so much to the hospital and to the area.

Mr. ANEURIN BEVAN said that probably one jealousy was driving out another. He was anxious for the local hospital to preserve its identity and its tradition within the National Health Service.

Mrs. E. M. BRADDOCK said some hospital management committees were anxious to get rid of the names by which the hospitals were called because under Public Assistance the hospitals had a very bad reputation for the treatment of patients.

Mr. BEVAN said he had known people anxious not to be sent into a particular hospital because it was called the Old Infirmary.

Fate of Kingston Victoria Hospital

Mr. J. A. BOYD-CARPENTER, on November 9, asked Mr. Bevan his decision as to the future of the Kingston Victoria Hospital.

Mr. BEVAN said this hospital was to be used as a gynaecological unit. The Surbiton Annexe hospital was to be converted to give alternative facilities to general practitioners.

Mr. BOYD-CARPENTER asked when the Surbiton Annexe was to be converted, and what was to happen to the 37 seriously ill patients before the conversion was completed.

Mr. BEVAN said arrangements were naturally being made for the patients. The Surbiton Annexe would be furnished as soon as the Ministry was aware that the general practitioners were prepared to make use of it.

Mr. BOYD-CARPENTER gave notice that he would raise the matter at the earliest opportunity.

Doctors' Prescriptions

Mr. GEORGE JEGER, on November 9, pointed out that doctors were having difficulty in resisting the demands of patients for prescriptions for medicinal preparations advertised direct to the public.

Mr. BEVAN said the responsibility for prescribing should rest solely on the judgment of the doctor. Sir Henry Cohen's Committee on Prescribing, therefore, recommended that publicly advertised preparations should not be prescribed under the National Health Service. This recommendation had been sent to all doctors, who had been asked to observe it. Any doctor who refused importunate demands had his full support.

Mr. HENRY STRAUSS asked whether it was a fact that far less than 1% of prescriptions had been for nationally advertised medicines.

Mr. BEVAN said he had not such precise information and would like to know its source.

Mrs. JEAN MANN asked if Mr. Bevan knew that many doctors were greatly perturbed at the wide latitude allowed for over-prescribing and that many asked for the reintroduction of the old procedure whereby prescriptions were properly scrutinized.

Mr. BEVAN believed this to be so, but remarked that it was a different question.

Food-poisoning.—5,329 cases of food-poisoning were notified to medical officers of health in the period January 1 to September 30, 1950.

Tricycles.—The number of persons waiting to be supplied with motor-propelled tricycles is 2,474. The average time of waiting is eight to ten months, but special action is taken to meet urgent needs. Output exceeds the current demand.

Tuberculosis Sufferer's Rations.—The priority food rations are three eggs a week and a double ration of butter or margarine, which at present gives an extra four ounces. Before June this year the weekly allowances were three eggs, an extra three ounces of butter or margarine, and an extra ounce each of cooking fat and bacon. When milk was controlled the priority supply was 14 pints a week.

Universities and Colleges

UNIVERSITY OF OXFORD

An Act of Congregation of the University of Oxford passed on October 31 altered the existing regulations so as "to include original work among the requirements for the degree of Master of Surgery and to adjust the requirements to meet the needs of a candidate who has specialized in any branch of surgery."

Congregation also agreed to accept a decree authorizing the acceptance of a grant of £2,240 from the Medical Research Council for research into the effect of injection of radioactive substances. This work will be in the hands of Dr. Janet Vaughan, Principal of Somerville College and chairman of the Oxford Regional Hospitals Board; it will be carried out in the Department of Pharmacology. A further £1,000 was accepted for research in penicillin and similar substances by Dr. W. H. Wilkins, St. Peter's Hall, in the Department of Botany.

UNIVERSITY OF CAMBRIDGE

The Council of the Senate has appointed Sir Lionel Whitby as one of the representatives of the University at the Home Universities Conference to be held on December 15 and 16.

UNIVERSITY OF EDINBURGH

Professor Ian Aird, professor of surgery in the University of London and director of the Surgical Unit, Postgraduate Medical School of London, will deliver a Macarthur Postgraduate Lecture on "The Surgical Exposure of the Pancreas" in the surgery lecture theatre, University New Buildings, Edinburgh, on Friday, December 15, at 2.30 p.m. Senior students and graduates in medicine are invited to attend the lecture.

SOCIETY OF APOTHECARIES OF LONDON

A course of ten postgraduate lectures on "Modern Methods of Diagnosis and Treatment" will be delivered in the Hall of the Society (Black Friars Lane, Queen Victoria Street, E.C.) from December 4 to 8 (both dates inclusive), at 3.30 p.m. and 5 p.m. each day. The fee for the full course is £2 2s.; for any two lectures on the same afternoon, 10s.; and for a single lecture, 7s. 6d. Details will be published in the "Societies and Lectures" column of the *Journal*.

The Services

The following have been mentioned in recognition of gallant and distinguished services in Malaya during the period January 1 to June 30, 1950: Colonels C. P. Chambers and P. F. Palmer, O.B.E., late R.A.M.C.; Lieutenant-Colonel K. H. Clark, Lieutenant-Colonel (Temporary) T. M. W. D'Arcy, Majors R. Paul and P. A. P. Webberley, M.B.E., and Captain (Temporary) V. J. Logan, R.A.M.C.

A *Supplement* to the *London Gazette* has announced the following awards:

Three Clasps to the Territorial Efficiency Decoration.—Colonel D. L. Kerr, O.B.E., T.D., R.A.M.C.

Two Clasps to the Territorial Efficiency Decoration.—Colonel R. Rutherford, O.B.E., T.D., and Major E. C. Ellis, T.D., R.A.M.C.

2nd Clasp to the Territorial Efficiency Decoration.—Major (Honorary Colonel) W. Barclay, M.C., T.D., R.A.M.C.

1st Clasp to the Territorial Efficiency Decoration.—Major (Honorary Lieutenant-Colonel) G. M. Warrack, D.S.O., O.B.E., T.D., R.A.M.C.

Territorial Efficiency Decoration and Three Clasps.—Major-General P. H. Mitchiner, C.B., C.B.E., T.D., K.H.S., R.A.M.C.

Territorial Efficiency Decoration and Two Clasps.—Major L. C. Lade, R.A.M.C.

Territorial Efficiency Decoration and 1st Clasp.—Lieutenant-Colonels S. G. de Clive-Lowe and T. H. Dockrell, Major R. H. Webber, M.B.E., and Captain (Honorary Major) L. F. Evans, R.A.M.C.

Territorial Efficiency Decoration.—Lieutenant-Colonel G. A. G. Mitchell, Majors A. F. Alsop, E. E. Evans, and I. C. A. D. P. Graham, and Captain (Honorary Major) D. J. A. Alban-Jones, R.A.M.C.

Medical News

World Health Organization

Dr. C. H. Hampshire has been re-elected chairman of the Expert Committee on the Unification of Pharmacopoeias. Other officers are Dr. R. Hazard (France), as vice-chairman, Dr. H. Flück (Switzerland), and Professor E. Fullerton Cook (U.S.A.). The main task of the committee, which has met regularly since 1947, is to prepare an international pharmacopoeia with a unified nomenclature. The *W.H.O. Pharmacopoeia*, which contains descriptions of over 200 drugs, has now been completed, and the French and English editions will be in circulation by the beginning of next year. A Spanish translation will follow.

Manchester Lectures on History of Medicine

The University of Manchester has for a long time wished to interest its students in the history of medicine, and the Medical Faculty has had its good intentions stimulated from time to time by requests which have come from the students themselves. The desire to give a course of lectures on the history of medicine was to some extent in conflict with a strong reluctance to add anything to the already overloaded medical curriculum, but an experimental scheme has now been started. It is proposed that four or five lectures should be given each session, some by members of the university and some by distinguished visitors. The lectures are not to be compulsory, and medical students in all years may attend, as well as members of the university staff. No attempt is being made to give a comprehensive course in the history of medicine, or a series of lectures, but each lecturer is invited to speak on a branch of medical history which is of particular interest to him. In the course of six years of medical study students should thus be able to listen to lectures on many aspects of medical history, and those who have a liking for this kind of knowledge will be stimulated to find out more for themselves. The inaugural lecture has been given by Dr. Charles Singer, whose subject was "Leonardo da Vinci as Anatomist, Physiologist, and Man of Science." It was very well attended and much appreciated. Other lectures during the session will be by Dr. William Brockbank, Mr. Geoffrey Keynes, and Sir Geoffrey Jefferson, F.R.S.

Liverpool Medical Institution

An ordinary meeting of the Liverpool Medical Institution was held on October 26, with the president, Dr. D. Johnston, in the chair. Professor J. H. Biggart read a paper on "Rheumatic Fever." Dr. C. Astley Clarke, Dr. I. Ansell, and Dr. S. E. Keidan contributed to the subsequent discussion.

William Hyde Award

The Research Board for the Correlation of Medical Science and Physical Education has awarded the William Hyde award to Mr. H. H. Newell, the engineering superintendent in charge of the rehabilitation workshop of Vauxhall Motors Limited. The award is in recognition of his skill and resource in developing a form of engineering occupational therapy. William Hyde, in whose memory the award was instituted by the Nuffield Trust, died in 1945. His concern for the future of the hospital services to a large extent led to the establishment of the Nuffield Provincial Hospitals Trust.

Ulster Paediatric Society

The Ulster Paediatric Society met on October 6 in Armagh, with Dr. Robert Marshall in the chair. A discussion on "The Care of the Child in the First Year at School" was opened by Professor A. C. Stevenson, Dr. Kathleen Corbett, and Professor F. M. B. Allen, who presented several aspects of the subject, upon which other members commented. After the meeting members and guests visited the Armagh observatory by invitation of the astronomer.

Leeds Joint Council on Industrial Health

The Leeds Joint Council on Industrial Health—the first joint council to be established in the country—has issued a brief annual report for 1949–50. Dr. Vaughan Jones, representing the Leeds Division of the B.M.A., is chairman of the council, and among the other participating organizations are the Leeds Chamber of Commerce, the Leeds Trades Council, and a number of trade associations and trade unions. Following a conference of joint councils held at Derby last year, at which Dr. Vaughan Jones was chairman, the Leeds Council have under consideration a proposal to carry out a survey to determine the likely implications of a full occupational health service; this project has been deferred, however, until the report of the Dale Committee on Industrial Health is available. The Leeds Council has also been preparing new model by-laws aimed at improving food-handling.

Innervation of the Kidney

The third general meeting of the Renal Association was held at the Ciba Foundation in London on October 26, when microscope slides were demonstrated and two papers read. Dr. de Muylder described his findings with Cajal's reduced silver staining, chiefly working with embryo and newborn mice and human foetal material. He said that he had found various types of swellings on nerve fibres which ran alongside the renal venules, and these swellings sometimes projected into the lumen of the vessel or even crossed it completely, so that blood was separated from nerve fibre by only a thin endothelial sheath. In older animals he had never found these structures, however; it was possible they had some chemosensory function. He said that he had virtually never found nerve cells within the kidney. Dr. El Asfoury, working with the adult rat and human necropsy material, was convinced that nerve cells, often grouped in microganglia and showing synaptic junctions, were present in profusion in the kidney, and offered the demonstrable persistence of nerve fibres and even the growth of new ones in nerve degeneration (section) experiments as supporting evidence. He attributed the difference between his results and those of some other workers to his use of special staining techniques which did not show up the collagen reticulum—a potent source of confusion—to careful and extensive photomicrography, and to the establishment of very precise criteria for the recognition of nerve cells and fibres. The papers were followed by a short discussion.

Sécurité Sociale—the French National Health Scheme

Dr. J. A. Huet, mayor of Asnières (Seine), spoke on October 24 at the Institut Français in London on the development since the end of the war of the French concept of a national health service. In spite of strong opposition from the medical profession (as many as 12,000 out of the 28,000 doctors in France had voted against it) a service was now functioning in a majority of the Departments in which doctors agreed to charge on a scale of fees judged equitable by a national commission, and the patients claimed back from the health service up to 80% of the charge to them of medical attention and treatment. Dr. Huet said the scheme was successfully balancing its budget and had been able to finance centres for lung and heart surgery and other specialties, to organize a blood transfusion service, and to equip many hospitals to a better standard than hitherto known in France. But while the care and facilities for treatment of the severely ill patient had thus been improved, the service had not benefited the "benign" illnesses in the same way; the emphasis was on hospital and clinic development rather than home care and the individual family doctor. Medicine had evolved from charity to group responsibility, and from the practice of individual workers to that of the team. He thought that the undeniable faults in the service would be eliminated in time.

Distribution of Cortisone in U.S.A.

An American firm manufacturing cortisone—Messrs. Merck—announces that it will be made available in the U.S.A. from about November 1 in general as well as hospital practice. The price is being reduced to $35 a gramme.

"Fifty Years of Medicine"

The issue of the *British Medical Journal* for January 7, 1950, was devoted to a historical survey of the progress of medicine in the last 50 years. Many readers suggested that this symposium should be republished in book form. It will soon appear as a well-designed book of about 330 pages, royal octavo in size, bound in cloth boards, and with 33 pages of illustrations on art paper. It will be on sale from the end of the month through booksellers, or direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, price 15s., post free.

Wills

Dr. V. J. Duigan, of Gorleston-on-Sea, left £9,368; Dr. R. M. Galloway, formerly M.O.H. for Bolton and for Dewsbury, £6,782; Sir Arthur Bagshawe, C.M.G., formerly Director of the Bureau of Hygiene and Tropical Diseases, £12,953 (he left £100 to the Royal Medical Benevolent Fund); Dr. T. G. Laslett, of Farnworth, Lancs, £18,573; Dr. F. M. Burnett, formerly of Sevenoaks, £12,283; Dr. A. G. E. Wilcock, of Ringwood, Hants, £9,426; Dr. R. J. Hutchinson, of Haslemere, Surrey, son of the late Sir Jonathan Hutchinson, £20,214; Dr. E. J. Martin, of Kirkby Lonsdale, Westmorland, £11,840; and Dr. S. E. Critchley, of Bolton, £27,555.

COMING EVENTS

Empire Rheumatism Council

The Empire Rheumatism Council (Tavistock House North, Tavistock Square, London, W.C.) has arranged a week-end postgraduate course to be held at the Hall of the Society of Apothecaries of London, Black Friars Lane, Queen Victoria Street, E.C., on Friday, Saturday, and Sunday, November 17, 18, and 19, with the following programme: November 17, 4.30 p.m., Dr. W. S. C. Copeman, "Fibrositis"; 5.30 p.m., Dr. Oswald Savage, "Cortisone and A.C.T.H. in the Rheumatic Diseases." November 18, 10 a.m., Dr. E. G. L. Bywaters, "Juvenile Rheumatism"; 11.15 a.m., Dr. G. D. Kersley, "Gout"; 2 p.m., Dr. H. J. Gibson, "Pathology of the Rheumatic Diseases"; 3 p.m., Dr. H. F. West, "Rheumatoid Arthritis"; 4.30 p.m., Dr. F. Dudley Hart, "Ankylosing Spondylitis." November 19, 10 a.m., Dr. H. A. Burt, "The Aims of Physical Medicine in the Treatment of Rheumatism"; 11.15 a.m., Mr. W. D. Coltart, "Orthopaedic Aspects of the Rheumatic Diseases." The fee for the course (limited to 100) is £2 2s., payable to the general secretary of the council at the above address.

British Tuberculosis Association

A meeting of the British Tuberculosis Association will be held at 26, Portland Place, London, W., on Friday, November 24, at 3.15 p.m., when there will be a discussion on "The Use of Mass Radiography." The speakers will include Dr. Peter Kerley, on the development of mass radiography schemes in Great Britain; Dr. Norman Smith, on dry bones and how to clothe them; and Dr. Owen Clarke, on the wider application of miniature radiography.

International Haemophilia Society

A general meeting of the society will be held on Sunday, November 26, at 34, Eccleston Square, London, S.W.1, at 2.30 p.m. Anyone interested, and particularly patients and their relatives, are welcome to attend.

Christian Medical Fellowship

The London Committee of the Christian Medical Fellowship has arranged a meeting to be held at the Royal Empire Society, Northumberland Avenue, London, W.C. (Craven Street entrance), on Tuesday, November 28, at 7.45 for 8.15 p.m., when Mr. H. J. Seddon will speak on "The Christian Heritage in Medicine." Further particulars may be obtained from Mr. D. F. Ellison Nash, 10, Kingswood Drive, Dulwich, London, S.E.19.

The Ophthalmological Society

The annual congress next year of the Ophthalmological Society will be held at the Royal Society of Medicine, 1, Wimpole Street, London, W.1, on March 29–31. The presidential address will be delivered by Mr. Maurice Whiting on March 29 at 10 a.m. The subject for discussion will be "The Association of Ocular and Articular Disease," which will be opened by Mr. L. H. Savin, Professor G. W. Pickering, Dr. F. Dudley Hart, Mr. A. B. Nutt, and Professor E. J. Wayne. Members who wish to take part in the subsequent discussion are advised to intimate their intention before the opening of the congress. No member may speak for more than ten minutes. The Bowman Lecture will be delivered by Sir Henry Dale, O.M., F.R.S. Members wishing to read a paper are asked to send the title, together with an abstract, to Mr. A. J. B. Goldsmith not later than December 31. Full particulars may be obtained from the society at 45, Lincoln's Inn Fields, London, W.C.2.

St. Mary's Hospital Medical School

The St. Mary's Hospital Medical School dinner for past and present students will be held at the Savoy Hotel (Embankment entrance), London, W.C., on Saturday, December 2, at 7 for 7.30 p.m., with Professor C. A. Pannett in the chair. Tickets, price 30s., may be obtained from the Medical School, Paddington, London, W.2.

Art Therapists in Clinics and Hospitals

A conference of art therapists in clinics and hospitals will be held on December 2, 1950, at 2 p.m., at 39, Queen Anne Street, London, W.1. The meeting will be short and will be mainly concerned with plans for future co-operation and training standards. The size of the conference is limited to 50. Applications will be dealt with in rotation by the conference secretary at this address.

Contraceptive Technique

A lecture and demonstration (on living models) on contraceptive technique will be given by Marie C. Stopes, Ph.D., at the Mothers' Clinic, 108, Whitfield Street, London, W., on Thursday, December 7, at 2.30 p.m. Tickets must be obtained in advance, as space is limited.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., November 17, 2.15 p.m., radiotherapy section meeting. Discussion: *"Radium Beam Therapy,"* to be opened by Drs. Constance Wood and A. A. Charteris.

Monday

HUNTERIAN SOCIETY.—At Apothecaries Hall, Blackfriars Lane, Queen Victoria Street, London, E.C., November 20, 8.30 p.m., discussion: *"That Heredity is more Fateful than is Environment,"* speakers, for the motion, Mr. J. H. Doggart and Mr. J. F. Eastwood; against the motion, Dr. J. A. Fraser Roberts and Professor J. B. S. Haldane, F.R.S.

●INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, London, W.C.—November 20, 5 p.m. *"Epilepsy,"* by Dr. D. Williams.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—November 20, 5.30 p.m., lecture-demonstration for postgraduates by Dr. E. Stengel.

KING'S COLLEGE, Strand, London, W.C.—November 20, *"Surface Reactions and Their Significance in Biology,"* by Professor E. K. Rideal, F.R.S.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—November 20, 3.45 p.m., *"Progressive Circulatory Failure,"* by Professor R. J. S. McDowall.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 20, 5 p.m., *"Paralytic Squint and Its Treatment,"* by Mr. T. K. Lyle.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—At the Concert Hall, the Y.W.C.A., Shakespeare Street, Nottingham, November 20, 5 p.m., *"Accident Prevention in the Home,"* public lecture by Dr. C. A. Boucher.

UNIVERSITY COLLEGE, Gower Street, London, W.C.—November 20, 4.45 p.m., *"Aspects of Protein Structure,"* by Dr. A. Elliott and Dr. W. E. Hanby.

Tuesday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., November 21, 5.30 p.m., *"Blood Groups,"* by Dr. R. R. Race, Ph.D.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 21, 5 p.m., *"Cutaneous Tuberculosis,"* by Dr. G. B. Dowling.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—November 21, 5.30 p.m., *"Some Aspects of Diseases of the Uveal Tract,"* by Mr. A. G. Leigh.

INSTITUTE OF UROLOGY (UNIVERSITY OF LONDON).—At St. Paul's Hospital, Henrietta Street, London, W.C., November 21, (1) 11 a.m., *"Cultivation and Identification of Pleuropneumonia-like Organisms: Principles of Bacterial Chemotherapy,"* by Dr. S. R. N. Bushby; (2) 5 p.m., *"Stricture of the Urethra,"* by Mr. J. F. Semple.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—November 21, 3.45 p.m., *"The Development of the Pharyngeal Derivatives and Endocrine Glands,"* by Professor J. D. Boyd.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 21, 5 p.m., *"Science and Art of Refraction,"* by Dr. T. H. Whittington.

UNIVERSITY COLLEGE, Gower Street, London, W.C.—November 21, 5.15 p.m., *"Chemical Transmitters,"* by Dr. W. S. Feldberg, F.R.S.

Wednesday

●BRITISH MEDICAL ASSOCIATION.—At B.M.A. House, Tavistock Square, London, W.C., November 22, 6.30 p.m., *"Can Disease Be Prevented?"* Sir Charles Hastings Lecture by Sir Lionel Whitby.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 22, 5 p.m., *"Medical Mycology,"* lecture-demonstration by Dr. R. W. Riddell.

INSTITUTE OF UROLOGY (UNIVERSITY OF LONDON).—(1) At Whittington Hospital, Highgate, N., November 22, 10.30 a.m., ward round by Mr. A. C. Morson; (2) at St. Paul's Hospital, Henrietta Street, London, W.C., November 22, 11 a.m., *"Local Diseases of the Penis,"* by Dr. A. H. Harkness; (3) at St. Paul's Hospital, Henrietta Street, London, W.C., November 22, 3.30 p.m., museum specimens by Mr. D. I. Williams; (4) at St. Paul's Hospital, Henrietta Street, London, W.C., November 22, 5 p.m., *"Prostatic Calculi,"* by Mr. H. K. Vernon.

RESEARCH DEFENCE SOCIETY.—At University College (Physiology Lecture Theatre), Gower Street, London, W.C., November 22, 5.30 p.m., *"Experiments on the Nervous System,"* Stephen Paget Memorial Lecture by Professor E. D. Adrian, O.M., F.R.S. Followed by annual general meeting of the society.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—November 22, 3.45 p.m., *"Sensations Associated with the Stomach,"* by Professor W. R. Spurrell.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 22, 4 p.m., *"Clinical Ophthalmology"* (Revision), by Mr. R. A. Burn and Mr. R. P. Crick; 5.30 p.m., *"Ophthalmic Neurology,"* by Mr. L. H. Savin.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—November 22, 3.30 p.m., *"The Advantages and Disadvantages of the Prefabricated House,"* by Mr. A. C. Bossom, F.R.I.B.A., M.P.

ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE, Anatomy Lecture Theatre, Charterhouse Square, London, E.C.—November 22, 5 p.m., *"The Reactions of Bacteria to Chemotherapeutic Agents,"* Kettle Memorial Lecture by Professor L. P. Garrod.

SOCIETY OF CHEMICAL INDUSTRY: FOOD GROUP.—At National Institute for Medical Research, The Ridgeway, Mill Hill, London, N.W., November 22, 6.15 p.m., meeting of Microbiological Panel. *"Recent Aids to the Study of Microbiology."* Papers by Sir Alexander Fleming, Dr. W. J. Elford, Mr. D. A. Tanfield, and Dr. W. H. Hughes.

Thursday

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C., November 23, 5.30 p.m., *"Blood Formation,"* by Dr. J. V. Dacie.

HONYMAN GILLESPIE LECTURE.—At University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh, November 23, 5 p.m., *"Differential Diagnosis in Acyanotic Congenital Heart Disease,"* by Dr. R. M. Marquis.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 23, 5 p.m., *"Pigmentary Conditions of the Skin,"* by Dr. I. Muende.

INSTITUTE OF OPHTHALMOLOGY, Judd Street, London, W.C.—November 23, 5.30 p.m., *"The Anatomy of the Ocular Muscle,"* by Dr. F. Stansfield.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—November 23, 3 p.m., *"The Rhinencephalon,"* by Professor F. Goldby.

INSTITUTE OF UROLOGY (UNIVERSITY OF LONDON).—At St. Paul's Hospital, Henrietta Street, London, W.C., November 23, (1) 11 a.m., *"Chancroid,"* by Dr. W. N. Mascall; (2) 5 p.m., *"Injuries, Fistula, and Foreign Bodies of the Urethra,"* by Mr. H. G. Hanley.

LIVERPOOL MEDICAL INSTITUTION.—At Royal Liverpool Children's Hospital, Myrtle Street, Liverpool, November 23, 3.30 p.m., clinical demonstration.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 11, Chandos Street, London, W., November 23, 3 p.m., film: "*Thrombosis and Embolism*," by Mr. Maurice Lee.

LONDON UNIVERSITY, Senate House, Bloomsbury, W.C.—November 23, 5.30 p.m., "*The Biological Aspects of War: Conduct*," by Professor F. A. E. Crew, F.R.S.

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., November 23, 8.15 p.m., "*The Case of Stanley Setty*," by Dr. F. E. Camps.

ROYAL ARMY MEDICAL COLLEGE.—At Lecture Theatre, John Islip Street, London, S.W., November 23, 5 p.m., "*Some Clinical Experiences During the Burma Campaign*," by Professor G. A. Ransome.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—November 23, 3.45 p.m., "*The Application of Biochemistry to Clinical Problems*," by Dr. N. Martin.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 23, 5.30 p.m., "*Operative Surgery*," by Miss J. M. Dollar.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—November 23, 4.30 p.m., lecture-demonstration on psychiatry by Dr. D. Curran.

TORQUAY AND DISTRICT MEDICAL SOCIETY.—At Torbay Hospital, November 23, 8.30 p.m., "*Medical Aspects of Hypertension*," by Dr. E. C. Warner.

Friday

KENT AND CANTERBURY HOSPITAL, Canterbury.—November 24, 8 p.m., clinical meeting.

●MAIDA VALE HOSPITAL MEDICAL SCHOOL, London, W.—November 24, 5 p.m., clinical neurological demonstration by Dr. Marion Greaves.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, London, W.—November 24, 8 p.m., "*World Health and Treponematoses*," by Dr. T. Guthe.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 24, 4.15 p.m., "*Pathology*," by Miss M. Savory.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—November 24, 8 p.m., "*Congenital Heart Disease*," dissertation by Mr. Ralph Shabetai.

Saturday

ROYAL DENTAL HOSPITAL OF LONDON; SCHOOL OF DENTAL SURGERY, Leicester Square, W.C.—November 25, 10 a.m. and 2 p.m., annual clinical "At Home"; 7 p.m., annual dinner at Savoy Hotel.

APPOINTMENTS

ALFORD, K. F., M.B., Ch.B., D.P.H., Deputy County Medical Officer, Norfolk

BATES, T. J. N., M.B., B.Ch., D.P.M., Non-resident Whole-time Psychiatrist, Winwick Hospital, Liverpool Regional Hospital Board.

HAWKINS, C. F., M.D., M.R.C.P., D.A., Assistant Physician to United Birmingham Hospitals.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*House-physician (Junior Registrar Grade)*, D. A. H. Trythall, M.D., M.R.C.P. *House-surgeon (Junior Registrar Grade)*, Irene M. S. Cade, M.B., B.S. *Junior Resident Anaesthetic Registrar (Junior Registrar Grade)*, J. A. Clarke, M.B., B.Ch.

INGRAM, H. VERNON, O.B.E., T.D., M.B., B.S., D.O.M.S., Ophthalmic Surgeon and Head of the Department of Ophthalmology, United Newcastle-upon-Tyne Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Eadie.—On November 10, 1950, at Brighton General Hospital, to Beryl (formerly Roberts), M.B., B.Ch., wife of Ronald Eadie, M.R.C.O.G., a daughter—Sarah Ann.

Eedy.—On October 31, 1950, at 86, Laurel Avenue, Forest Town, Mansfield, Notts, to Mrs. Eedy (formerly Chanu), wife of Dr. B. N. Eedy, a brother for Bernardine—Patrick.

Gilsenan.—On November 6, 1950, at 46, Waverley Road, St. Albans, to Tessa, wife of Dr. B. M. C. Gilsenan, a daughter—Clare Margarita Maria.

DEATHS

Blair.—On November 10, 1950, at 3A, Eton Terrace, Edinburgh, David Blair, M.D.

Briggs.—On November 2, 1950, at Auckland, New Zealand, Isaac George Briggs, M.R.C.S., L.R.C.P., aged 58.

Daniel.—On November 7, 1950, at 2, Hampstead Hill Gardens, London, N.W., Sir Augustus Moore Daniel, K.B.E., Hon.Litt.D., M.B., aged 83.

Fletcher.—On November 4, 1950, at Rustington, Henry James Fletcher, M.B., C.M., Lieutenant-Colonel, R.A.M.C., retired, aged 90.

Groves.—On November 8, 1950, at his home in London, Charles Nixon Groves, C.B.E., M.D.

Harrison.—On October 26, 1950, Alexander Thomas Harrison, M.B., B.S., of Park House, Sherburn, Durham.

Haworth.—On November 4, 1950, Henry Dean Haworth, M.D., D.P.H., of Edgefield, Nelson, Lancs, aged 69.

Ilderton.—On November 7, 1950, at Homefield, Meopham, Kent, Colin Ilderton Ilderton, M.B., B.S., aged 66.

Jameson.—On October 31, 1950, at Eldoret Hospital, Kenya, Ernest Tooke Jameson, M.D., of Cheveya, Turbo, Kenya.

Kilner.—On November 5, 1950, suddenly, at R.A.F. Hospital, Fayid, Egypt, Hugh Pomfret Kilner, M.B., B.Chir., Flying Officer, R.A.F., aged 26, son of Professor T. Pomfret Kilner and the late Olive Mary Kilner, and stepson of Mrs. T. P. Kilner, White Lodge, Old Headington, Oxford.

MacLachlan.—On October 26, 1950, at the Western Infirmary, Glasgow, John Thomson MacLachlan, M.D.

Smith.—On November 10, 1950, at Leages Hospital, Newcastle-upon-Tyne, Andrew Smith, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., of Leven House, Swalwell, Co. Durham, aged 68.

No. 43

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended October 28.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1950 (a)	(b)	(c)	(d)	(e)	1949 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Meningococcal infection	32	2	15	1	—	26	2	7	—	2
Deaths		—	—				1	—		
Diphtheria	40	3	17	2	1	101	11	33	4	4
Deaths	1	—	—	—	—	—	—	—	—	—
Dysentery	241	19	144		—	139	13	55	—	—
Deaths		—			—				—	—
Encephalitis, acute	9	1	—		—	1	—	—	—	1
Deaths		—		—			—			
Erysipelas			22	9	2			15	11	5
Deaths							—			
Infective enteritis or diarrhoea under 2 years				40	16				55	
Deaths	7		1	4	1	31	—	7	6	—
Measles*	6,632	471	116	95	98	995	63	27	129	45
Deaths†		—	—	—	—			—	—	—
Ophthalmia neonatorum	27	1	8		1	39	4	7	—	—
Deaths										
Paratyphoid fever	14	1	—		—	14	1	1 (B)	2 (B)	—
Deaths	—		—		—	—	—	—	—	—
Pneumonia influenzal	435	24	1		8	303	18	—	4	4
Deaths (from influenza)‡	17	6	—	—	—	11	2	3	—	—
Pneumonia, primary	141	24	115	¶ 8	9	136	15	133	10 7	7
Deaths										
Poliomyelitis, acute	253	14	25	3	5	367	55	5	5	4
Deaths§	12	—		—		21	2			
Puerperal fever			12				—	6		
Deaths										
Puerperal pyrexia‖	78	12	7		1	72	4	6	—	—
Deaths							—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,141	98	200	87	48	1,972	169	224	99	159
Deaths†		—	—	—	—			—	—	—
Smallpox	—	—	—		—	—	—	—	—	—
Deaths					—				—	—
Typhoid fever	6	1	1	2	2	7	—	—	2	—
Deaths	—	—	—		—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths					—				—	—
Whooping-cough	3,077	295	307	82	29	749	31	45	50	39
Deaths	1	—	—	—	—	2	—	—	—	—
Deaths (0–1 year)	212	37	25	15	7	233	30	38	23	6
Deaths (excluding stillbirths)	4,360	707	555	191	92	4,466	710	577	157	118
Annual death rate (per 1,000 persons living)			11·1					11·6	9·7	
Live births	6,561	1080	814	352	236	6,699	1051	820	376	177
Annual rate per 1,000 persons living			16·4					16·4	23·3	
Stillbirths	169	24	32			150	20	29		
Rate per 1,000 total births (including stillborn)			38					34		

* Measles is not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

¶ Primary pneumonia no longer notifiable in Eire.

EPIDEMIOLOGICAL NOTES

Poliomyelitis

Notifications of poliomyelitis in the week ending November 4 were: paralytic, 147 (182); non-paralytic, 57 (71); total, 204 (253). The figures for the previous week, compared with which there was a drop in the total notifications of 49, are in parentheses. Notifications for the corresponding week in 1947 and 1949 were 243 and 330.

Total uncorrected notifications for 1950 to and including the week under review are 7,747. The corresponding figures for 1947, 1948, and 1949 are 8,265, 2,050, and 5,589 respectively. Biggest decreases compared with the preceding week in county areas were as follows: Devon, 7; Durham, 6; Lancashire, 8; Norfolk, 5; Northumberland, 5; Worcester, 7. Any increases in notifications were comparatively insignificant and were widely scattered. In 24 counties there were no notifications at all. The weekly decrease in notifications is well maintained.

Discussion of Table

In *England and Wales* increases were recorded in the number of notifications of measles 756, whooping-cough 403, dysentery 72, and decreases were reported for scarlet fever 86 and acute poliomyelitis 25.

The largest increases in the number of notifications of measles were Yorkshire East Riding 129, London 105, Glamorganshire 96, Surrey 83; the only large decrease was Yorkshire West Riding 93. The largest fluctuations in the trends of scarlet fever were a decrease of 34 in Lancashire and an increase of 17 in London. The chief feature of the returns for diphtheria was an increase of 5 in the notifications in Yorkshire West Riding due to an outbreak of 4 cases in Rotherham R.D. The largest rises in the local trends of whooping-cough were Lancashire 98, Surrey 72, and London 44.

The chief centres of dysentery were Leicestershire 38 (Leicester C.B. 37); Yorkshire West Riding 31 (Huddersfield C.B. 15); Cumberland 27 (Penrith R.D. 25); Essex 26 (Romford M.B. 19); London 19 (Chelsea 8); Lancashire 18 (Liverpool C.B. 7); Kent 13; Yorkshire North Riding 12 (Middlesbrough C.B. 12); Gloucestershire 11 (Cheltenham M.B. 9); Durham 11.

The largest returns for acute poliomyelitis were Lancashire 22 (Liverpool C.B. 4); Devonshire 17 (Plymouth C.B. 4); Warwickshire 16 (Birmingham C.B. 13); Yorkshire West Riding 16 (Leeds C.B. 5); London 14; Gloucestershire 12 (Bristol C.B. 9); Staffordshire 11; Durham 10.

In *Scotland* decreases were recorded in the number of notifications of measles 24 and acute primary pneumonia 26, and an increase of 33 was reported for dysentery. The largest returns of dysentery were from the cities of Glasgow 69, Edinburgh 25, and Dumfries 11. The notifications of acute poliomyelitis were 4 fewer than in the preceding week; the largest returns were Glasgow 7 and Dundee 4.

In *Eire* an increase occurred in the number of notifications of whooping-cough 28 and diarrhoea and enteritis 12, and a decrease was reported for measles 19. In Dublin C.B. a rise of 11 for scarlet fever was recorded.

In *Northern Ireland* an increase of 42 in the notifications of measles and a decrease of 11 for diarrhoea and enteritis were the chief features of the returns. The largest rise in measles was 27 in Armagh county.

Week Ending November 4

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,108, whooping-cough 3,087, diphtheria 49, measles 7,815, acute pneumonia 433, acute poliomyelitis 204, dysentery 260, and paratyphoid fever 5.

Dr. T. M. Montford, of Castle Donington, near Derby, deputy chairman of the Leicestershire and Rutland Executive Council and ex-chairman of the local medical committee, has been re-elected from the Midland Division for the third year in succession to the management committee of the Association of Executive Councils.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Pressure Cooking and Vitamins

Q.—*Is it true that essential vitamins are destroyed to a greater extent in pressure cooking than in the usual method of cooking food?*

A.—The chief factors in cooking which affect the retention of the less stable vitamins, such as vitamins B_1 and C, are the temperature, the time, the presence of air, and the amount of cooking water. The higher temperature reached in pressure cooking would tend to increase the loss of these vitamins, but the shorter time, the rapid elimination of air, and the small amount of cooking water would tend to decrease the loss. Only by experiment has it been possible to determine what the total effect is. One series of such experiments was reported in the *Journal* by Chappell and Hamilton (1949, **1**, 574), and these were the subject of a leading article (*Journal*, 1949, **1**, 582). These authors found that, with careful pressure cooking, there was less loss of vitamins B_1 and C in vegetables than with the most careful method of ordinary cooking. Similar results were found by Thomas *et al.* (*J. Amer. diet. Ass.*, 1949, **25**, 39) for vitamins B_1 and C and riboflavin, and by Hewston *et al.* (*Misc. Publ. U.S. Dep. Agric.*, No. 628, 1948) for vitamin C.

The short answer to the question, then, is that the vitamins are destroyed to a *lesser* extent in pressure cooking than in the usual methods of cooking.

Cervical Erosion

Q.—*What local treatment, other than cauterization, would you recommend for cervical erosions?*

A.—Cervical erosion in itself is not necessarily pathological and may not require any treatment. There is evidence that it is present at birth in about one-third of female babies, and it can presumably persist to adult life. This is a possible if not probable explanation of its occurrence in virgins. If erosion develops only in relation to pregnancy, it not infrequently disappears spontaneously during the months following delivery. Only when there are good grounds for believing that the erosion is secondarily infected, or is definitely producing symptoms, is treatment really necessary, and the best is cauterization. The use of chemical caustics such as silver nitrate or zinc chloride has been largely abandoned, and the actual cautery or diathermy coagulation is generally preferred. In bad cases diathermy conization or knife excision of the affected area is occasionally justified.

Endocrine therapy or the local application of antiseptics and astringents is of little, if any, value.

Athleticism and Longevity

Q.—*Is there anything known about the effects of athleticism on longevity? I have heard it stated that athletic people degenerate early and are more prone to heart trouble, etc., in middle life.*

A.—There is no support for the idea that strenuous athletics in youth lead to degenerative changes in the cardiovascular system in later life. Accepting as criteria the maintenance of unimpaired health and longevity, there is considerable evidence to the contrary.

J. Plesch (*Lancet*, 1932, **1**, 385) in an article on the subject of arteriosclerosis asserted that most athletes die before the age of 50 and that they are seldom capable of great physical exertion when they attain middle life. In the course of an ensuing correspondence Plesch explained that he had in mind certain pathological conditions and that under the term "athlete" he comprehended occupations which carried

hazardous associations—e.g., copper mining—an elasticity of terminology which was surely inadmissible. He referred also to an excessive mortality among stage acrobats, which might very well be true.

On the other hand, a great deal of information relating to athletes in the true sense of the word is available to allay such misgivings. Taking the university boat race (which represents an extreme form of violent exertion), John Edward Morgan, the Manchester physician, published in his work *University Oars* (1873, Macmillan) his elaborate inquiry into the after-histories of those who had rowed in the race between 1829 and 1869. In all, 294 were investigated, 40 having died. It emerged from this study that the life expectation of those who had taken part in the race was nearly five years longer than that of those accepted for life insurance.

Meylan in 1904 (*Harvard Graduates Magazine*, 1903–4, **12**, 362, 367, and 543) undertook a similar investigation among Harvard oarsmen between 1852 and 1892 with almost identical results. More recently Cooper and his colleagues (*Med. J. Aust.*, 1937, **1**, 577) found that, of 100 oarsmen at Ormond College, Melbourne University, 17 had died from natural causes during the succeeding 50 years. The expected mortality of men of the average age of 21 over the same period was, as quoted by the Australian Mutual Provident Society, 31.8%. Hartley and Llewellyn (*British Medical Journal*, 1939, **1**, 657), from a study of those who rowed in the Oxford and Cambridge boat race from 1829 to 1928, concluded that the expectation of life of the university oarsmen was appreciably better than that of the assured lives of their own generation, but that more recently this superiority had tended to diminish. Unfortunately no such investigations appear to have been conducted upon track athletes.

Without wishing in any way to put forward a case that athleticism contributes to longevity, it suffices for the present purpose dogmatically to deny the reverse.

Saccharin and Cancer

Q.—*There is a widely held opinion that saccharin is a carcinogen. Is this true?*

A.—There is no evidence that saccharin is a carcinogen for either man or animals. "Dulcin" (paraphenetyl-urea), one of the other artificial sweetening agents, has been shown to cause cancer of the liver in animals when the food contained 0.1% (*Fed. Proc.*, 1950, **9**, 272).

Harvesters' Lung

Q.—*What is the condition known as "harvesters' lung"?*

A.—Harvesters' or farmers' lung is a pneumonic process occurring in persons handling hay or grain. It is due to infection of the lungs by fungi (aspergillus or penicillium moulds). The incidence is seasonal and appears to be related to the occurrence of mould in the hay or grain which develops as a result of inclement weather. J. M. Campbell (*Journal*, 1932, **2**, 1143) describes five cases occurring in Westmorland in the summer of 1931. Owing to unusual summer rainfall this was a poor season for hay-making. The persons affected were farmers or farm labourers previously in good health. They were aware of slight shortness of breath for several weeks. After definite exposure to moulds, such as when cleaning out hay from a barn, they experienced a sudden onset of extreme dyspnoea, cyanosis, cough, and mild pyrexia (100° F.—37.8° C.).

R. Fawcitt (*Lond. Hosp. Gaz., clin. Suppl.*, June, 1940) reports similar symptoms in hay-workers and grain-workers. Examination of the chest revealed diffuse areas of dullness to percussion, with crepitations, rales, and rhonchi in both lungs. Haemoptysis occurred occasionally, and micro-fungi were found in the sputum.

Results of treatment with sulphonamide drugs and antibiotics have been disappointing. The majority of cases are cured by rest in bed and the administration of potassium iodide in increasing doses up to 300 gr. (20 g.) daily. A few cases progress to cavitation and bronchiectasis with copious purulent sputum.

Rectal Prolapse

Q.—*Is there any treatment which can help a rectal prolapse of 40 years' duration in a man of 76?*

A.—The advice given on the treatment of this case depends upon how large the prolapse is—whether it is a complete prolapse of the whole thickness of the rectal wall or whether of the mucous membrane only. Also, in a man of this age, treatment will depend upon the presence or otherwise of urinary obstruction, which, if present, would have to be dealt with. If there is prolapse of mucous membrane only, then submucous injections of 5% phenol in oil is often a good palliative treatment. If the prolapse is a complete one, but only small (not more than 1 in. (2.5 cm.) in extent), then the insertion of a silver wire around the anus (Thiersch's operation) might afford relief.

Falling Hair and Lactation

Q.—*Why does the hair of some women fall out easily and almost cease to grow during lactation? Can this be prevented?*

A.—There are no doubt different reasons for the fall of hair in different patients during lactation. The fall in oestrogen level after parturition is probably a major factor, though stress and strain, anaemia and debility, which are also commonly present, may play some part.

Treatment of the contributing factors is symptomatic, but it is probably unwise to interfere with the oestrogen balance at this stage. The falling of the hair is almost a normal happening, and recovery is the rule.

Herpes Simplex

Q.—*How should recurrent herpes simplex be treated?*

A.—Herpes simplex is due to a virus. It seems probable that the virus resides in the skin or mucosae and, although it may give rise to an eruption without any obvious exciting cause, fever often stimulates it to activity. Some patients have recurrent attacks over many years. Treatment is ineffectual, although some claim the eruption heals more rapidly if alcohol is applied to it. Untreated, the lesion disappears in about a week. The only prophylactic measure worth trial is vaccination with killed vaccinia virus, repeated three times; this has been successful in preventing the recurrent variety.

NOTES AND COMMENTS

Red Perspiration.—Dr. A. L. LEIGH SILVER (Porton) writes: I think it worth while noting that apparent red perspiration ("Any Questions?" November 4, p. 1072) can be caused by dye from outer garments, even if these are not red. This may be due to a selective action by sweat on this pigment. Secondly, a true red perspiration may be caused by the excretion of certain industrial chemicals. Trinitrotoluene gives sweat a reddish colour and this may show quite a bright red on clothing if there is a little residual alkali on it. I do not think that staining from untreated fungal infections is common. I have never noted it in trichomycosis (yellow, black, or red varieties).

Agents for Publishers.—Messrs. H. K. Lewis and Co., 136, Gower Street, London, W.C.1, state that they are the London agents for the Yearbook Publishers, publishers of *The Antihistamines*, by S. M. Feinberg, M.D., which was reviewed in the *Journal* of November 4 (p. 1040).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London*. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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